CLINICAL SPECTRUM AND SHORT-TERM OUTCOME OF ACUTE MYELOID LEUKEMIA PATIENTS

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Dedicated

to

my Parents

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Dr Gurinderjit Singh

LIST OF ABBREVIATIONS

ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
APML	Acute promyelocytic leukemia
ATO	Arsenic trioxide
ATRA	All trans retinoic acid
CHIP	Clonal hematopoiesis of indeterminate potential
CNS	Central nervous system
CR	Complete remission
CVS	Cardiovascular system
DAMA	Discharged against medical advice
EF	Ejection fraction
FAB	French-American-British
GM-CSF	Granulocyte macrophage colony stimulating factor
GVHD	Graft versus host disease
HB	Hemoglobin
HCT	Hematopoietic cell transplantation
HiDAC	High dose cytarabine
HSC	Hematopoietic stem cells
ICH	Intracranial hemorrhage
INR	International normalized ratio
LDH	Lactate dehydrogenase
LSC	Leukemia stem cells
LVEF	Left ventricle ejection fraction

MDS	Myelodysplastic syndrome
NGS	Next generation sequencing
OS	Overall survival
PTI	Prothrombin time index
SBP	Systolic blood pressure
SD	Standard deviation
SPO2	Oxygen saturation
TLC	Total leucocyte count
TRF	Treatment related mortality
VEGF	Vascular endothelial growth factor
WHO	World health organization

ABSTRACT

Introduction: Acute myeloid leukemia (AML) is collection of neoplastic blood disorders categorized by the proliferation and growth of immature hematopoietic cells in the bone marrow and blood. The higher incidence of AML is seen in adults, accounting for almost 80 % of acute leukemia in adults and only 20 % of acute leukemia in children. It is most commonly found acute leukemia in adults. AML is actually a varied selection of wide number of malignant neoplastic diseases that may be grouped on the basis of morphological, cytogenetic and also with molecular and genetics criteria.

Aim of Study: To study the clinico-pathological spectrum and short-term outcome of acute myeloid leukemia patients admitted in a tertiary care hospital.

Materials & methods: Patients over 18 years with acute myeloid leukemia admitted to the Department of Medicine and Allied Specialties at Dayanand Medical College and Hospital (DMCH), Ludhiana, were included in a prospective observational study from 1st October 2022 to 31st March 2024. Outcomes measured included length of hospital stay, clinical, laboratory, and treatment profiles, documentation of hematologic and bone marrow remission, treatment outcomes (standard or supportive care), and a 3-month post-discharge follow-up. Necessary investigations included basic (CBC, LFT, RFT, urine routine, ESR, LDH, CRP), specific (bone marrow aspiration and biopsy, molecular analysis via PCR or next-generation sequencing), and radiological (chest radiograph, US, CT Scan, MRI, PET scan). Ethical clearance was obtained (attached).

Results: The AML study found the median age of patients was 54 years (IQR: 37-66). Respiratory infections were documented in 34% on HRCT chest, with 78% having normal LVEF and 4% systolic dysfunction. Common markers included CD13 (70%) and CD117 (68%), with NPM-1 detected in 16%. Subtypes M2 (28%) and M4 (24%) were most common. Treatments included hypomethylating agents (54%) and intensive chemotherapy (12%), with 38% achieving bone marrow remission. Outcomes: 64% discharged, 28% left against medical advice, and 8% died. Three-month follow-up showed 50% on regular follow-up, 32% deceased, 12% lost to follow-up, and 6% relapsed. Non-M3 patients had higher mortality (57.5%) and loss to follow-up, while M3 patients had better follow-up rates (60%). Median survival time was 156 days, highlighting the need for tailored therapeutic approaches.

Conclusion: The findings underscore the challenges in managing AML patients in a resource constrained nations, particularly the high early mortality rates. By identifying specific genetic profile and their associations with AML subtypes, the study offers valuable information that can guide personalized treatment strategies, ultimately aiming to improve patient outcomes.

Keywords: Prospective, Acute Myeloid Leukemia, Clinical spectrum, Short term outcome in adult patients

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INTRODUCTION

Carcinogenesis is the progressive development of benign tissue into an asymptomatic preneoplastic condition, which ultimately transforms into malignancy. The progression of somatic cells to neoplastic clones, which possess pathological characteristics such as aberrant cell proliferation, resistance to apoptosis and differentiation, and immune-evasion mechanisms, is facilitated by the sequential acquisition of genetic alterations, including copy number variations, chromosome rearrangements, and gene mutations, in addition to early epigenetic modifications. The thorough investigation of preneoplastic stages may unveil novel targets for early therapeutic intervention, which has significant ramifications for the comprehension of cancer biology and evolution.[1]

Bone marrow is among the most rapidly proliferating tissues in the human body, with an estimated daily production of one trillion mature blood cells.[2] Asymmetric cell divisions of hematopoietic stem cells (HSCs) generate more differentiated cells and contribute to the maintenance of an HSC pool. These cells will transform from progenitors to the mature cells and compounds of our circulatory system—specifically, erythrocytes, thrombocytes and lymphocytes—via a series of meticulously coordinated maturation processes.[3] Neoplastic clones may arise from pluripotent human stromocytes (HSCs) or more differentiated myeloid or lymphoid progenitor cells. In addition to the cell of origin, the acquired genetic and epigenetic modifications may influence the phenotype of the resulting malignancy.[4]

Leukemias are a group of malignant disorders of the haemopoietic tissues which are frequently characterized by an increased number of leucocytes in the blood or a heterogeneous assemblage of neoplasms resulting from the malignant metamorphosis of haemopoietic cells. Leukemic cells predominantly proliferate in lymphoid and bone marrow tissues, where they disrupt regular hemopoesis and immunity. They ultimately pass through the periphery of the circulation and infiltrate

various tissues. Therefore, leukemia is a progressive and ultimately fatal disease, with hemorrhage or infections being the leading causes of mortality. Depending on the nature of the course, its duration can range from a few days or weeks to several years.[5] Leukemia comprises a mere 0.15–0.6% of the overall medical admissions in numerous general hospitals across India. Males are more commonly affected than females. The male-to-female ratio is 3:2 in acute leukemia. 20–25% of leukemia cases in India are caused by AML, while 15–25% are caused by ALL. AML and ALL have respective annual incidence rates of 5.6 and 30.9 per million individuals. Acute lymphoblastic leukemia primarily affects adolescents and young adults, while acute myeloid leukemia (AML) predominantly affects adults.[6]

Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy that causes impaired production of normal blood cells due to clonal expansion of myeloid blasts in the bone marrow, peripheral blood, and/or other tissues. Thus, infiltration of leukemic cells into the bone marrow inevitably results in bone marrow failure manifesting as anemia or thrombocytopenia, whereas, dependent on the total white cell count, the absolute neutrophil count may be low or normal.[7] A maturational arrest of bone marrow cells during their nascent phases constitutes the pathophysiology underlying AML. While the precise mechanism underlying this arrest is still being investigated, it frequently entails the activation of aberrant genes via chromosomal translocations and other forms of genetic abnormalities. Such genetic modifications may be acquired through inheritance or exposure to environmental insults.[8,9]

It has been documented that the incidence and subtype of AML vary geographically. Asia and Latin America have the lowest incidence of AML in adults, whereas North America, Western Europe, and Oceania have the highest incidence. Asia has the highest incidence of pediatric AML, while North America and India have the lowest.[10] AML constitutes around 80% of acute leukemia in adults and 20% of acute leukemia in

infants. Age is a progressive determinant of the incidence of acute myeloid leukemia (AML); in adults aged 65 and above, the incidence is roughly thirty times greater than that observed in children. Asia has the highest incidence of pediatric AML, while North America and India have the lowest. The annual incidence of new cases of AML was 4.2 per 100,000 men and women, according to the SEER database. Annual mortality was recorded at 2.8 per 100,000 males and females. These rates are age-adjusted and depend on cases and fatalities from 2010 to 2014. Diagnosis of AML is most prevalent in individuals aged 65–74 years. When diagnosed, the median age is 68 years.[11]

The antecedent hematologic disorder that is most frequently observed is myelodysplastic syndrome, which serves as the most prevalent risk factor for AML. Congenital disorders such as neurofibromatosis, Bloom syndrome, Down syndrome, congenital neutropenia and Fanconi anemia are risk factors for AML. Although the onset of AML in these patients is typically during childhood, a minority may manifest in young adulthood. The ingestion of benzene, smoking and radiation have all been identified as risk factors for AML. As the survival rate of cancer patients with primary malignancies improves, there is a concurrent rise in the incidence of AML due to the administration of chemotherapeutic agents. As an illustration, at the 5-year mark, the cumulative incidence of acute leukemia among breast cancer patients who received adjuvant therapy consisting of doxorubicin and cyclophosphamide was between 0.2 and 1%.[12]

Patients who have undergone prior chemotherapeutic agent exposure can be categorised into two groups: (1) individuals who have been exposed to alkylating agents, and (2) individuals who have been exposed to topoisomerase-II inhibitors. Individuals who have been previously treated with topoisomerase-II inhibitors do not experience a myelodysplastic phase. Cytogenetic analysis demonstrates the presence of a translocation involving band 11q23. Patients with less frequent

occurrences of leukemia also exhibited balanced translocations, including inversion 16 or t(15;17). For alkylating agents and radiation exposure, the average latency period between drug exposure and acute leukemia is three to five years; for topoisomerase inhibitors, it is only nine to twelve months.[13]

Induction is administered to non-M3 cells using primarily daunorubicin and cytarabine. Daily infusions of 45–90 mg/m^2 of daunorubicin are administered from day 1 to day 3, whereas daily infusions of 100–200 mg/m^2 of cytarabine are administered over seven days. Recent research has unequivocally demonstrated that a dose of 60 mg/m2 is superior to 45 mg/m^2, and Burnett et al. have further demonstrated that 60 mg/m2 is superior to 90 mg/m^2 in terms of maintaining complete remission (CR) and reducing 60-day mortality. Idarubicin can be utilised in lieu of daunorubicin to achieve an equivalent result. CR rates in the age group of less than 50 years have maintained a consistent range of 60%–70% in the largest cooperative group trials of anthracyclines and infusional cytarabine. After documentation of remission, consolidation ensues subsequent to induction. The treatment modality is determined primarily by risk stratification. Patients at adverse risk are selected for allogenic stem cell transplantation. Patients deemed to be at low risk should undergo three to four cycles of high-dose cytarabine. Patients at intermediate risk shall receive highdose cytarabine or an allogenic stem cell transplant, the choice of which is contingent on the donor's availability and the patient's age. As an induction therapy, patients with M3 acute promyelocytic leukemia [APML] require a differentiating agent. These substances are arsenic trioxide and transretinoic acid (ATRA), both of which are combined with conventional chemotherapy agents. The majority of investigations report a CR rate of approximately 90%. Transplantation is reserved for relapsed patients only. Consideration should be given to allogeneic stem cell transplantation for eligible candidates.[14]

Developing nations bear an enormous burden of cancer, particularly haematological malignancies, as a result of urbanisation, population growth, ageing and shifting dietary patterns, improved infection control and rising tobacco use. In a resource-constrained environment such as our nation, epidemiological data pertaining to this critical haematological malignancy are scarce. The purpose of this research is to identify the clinical manifestations, pathological range, and short term prognosis of acute myeloid leukemia (AML) in patients who are admitted to a tertiary teaching hospital.

AIMS AND OBJECTIVES

To study the clinico-pathological spectrum and short-term outcome of acute myeloid leukemia patients admitted in a tertiary care hospital.

REVIEW OF LITERATURE

Acute myeloid leukemia (AML) constitutes approximately 80% of all cases of leukemia in adults, making it the most prevalent form. Immature "blast cells" proliferate clonally in the peripheral blood and bone marrow, causing erythropoiesis to be rendered ineffective and bone marrow to fail. Cure rates for patients aged 60 years and above have increased by as much as 15%, while they have increased by about 40% for patients aged below 60 years due to recent developments in management guidelines. Despite therapeutic regimen advancements, the geriatric continue to have a dismal prognosis.[15]

Pathogenesis of AML

AML can be recognized by the aberrant proliferation and differentiation of myeloid precursors in the bone marrow, which constitutes its heterogeneous biology. AML is caused by a clonal process that arises from a transformed HSC and precedes the development of leukemia; it is characterized by clonal proliferation and affects otherwise healthy individuals. In healthy individuals, recurrent AML-associated mutations may accrue in hematopoietic progenitor cells as they age. This accumulation may result in clonal hematopoiesis of indeterminate potential (CHIP), which is characterized by clonal growth but no leukemia development.[16] A proliferative advantage enables these cells to proliferate while preserving regular hematopoiesis. The estimated annual progression rate from clonal hematopoiesis to acute myeloid leukemia (AML) is 0.5–1%. Age-related clonal hematopoiesis is differentiated from preAML by several factors: the quantity of mutations per sample, an increased frequency of variant alleles and mutations in particular genes, including DNMT3A, TET2, SRSF2 and ASXL1.[17]

Early HSCs undergo initiating leukemic mutations, which induce modifications in the process of self-renewal. The mutant HSCs' acquired capacity for self-renewal permits the gradual acquisition of additional mutations, the formation of leukemia stem cells (LSCs), and the possibility

of leukemia transformation. Originally defined with the functional capacity to induce leukemia in a NOD/SCID mouse, the LSC is defined in a manner analogous to that of the HSC, encompassing self-renewal capability, multipotence, and exceptional proliferative properties.[18] Insofar as class 1 mutations influence cell proliferation and class 2 mutations influence differentiation, the historical "two-hit hypothesis" of AML development is implicated by the possibility that the acquisition of additional mutations could impair differentiation. The precise permutation combinations that culminate in leukemogenesis are impacted by the mutual exclusivity and biological cooperation among particular mutated genes, aspects that have become more precisely delineated with the advent of more comprehensive next-generation sequencing (NGS) techniques in the past decade. The prognostic importance of specific mutations was affected by the existence, nonexistence, and potential collaboration with additional driver mutations. An increase in stem cell fitness due to early mutations may result in the subsequent acquisition of AML-specific mutations and the subsequent development of AML. An extensive quantity of mutated genes and patterns of cooperation are observed.[19]

Numerous elements contribute to the creation of a microenvironment that is conducive to the development of leukemia. This is characterized by aberrant cytokine signaling, immunosuppression and cell adhesion. This niche development may be influenced by age-related vascular changes, including an expansion of perivascular capillaries, an increase in PDGFRB-positive perivascular cells, the formation of arterioles and a surge in cellular stem cell factor.[20] thereby modifying the interaction of stem cells in the microenvironment of bone marrow. LSC development is also influenced by additional interactions of AML with the vascular niche, including E-selectin, VEGF/VEGFR, Notch signaling and GM-CSF secretion. AML development is also dependent on LSC interactions with osteoblasts, osteoclasts and mesenchymal stromal cells;

AML cells can differentiate into mesenchymal stromal cells to further support a permissive niche.[21]

Additionally, the inflammatory microenvironment has been linked to the development of AML. As an example, people afflicted with CHIP and TET2 mutations exhibit a heightened concentration of interleukin-8; this elevation has been associated with various ailments, such as atherosclerosis and cardiac disease. A pro-inflammatory phenotype was observed in mice with Tet2 deletion, as evidenced by elevated levels of interleukin-6, interleukin-1B and interleukin-8, as well as an accelerated development of atherosclerosis. There is an association between chronic inflammation and ageing. Individuals who have VEXAS syndrome, a systemic inflammatory condition distinguished by somatic mutations in UBA1, vacuoles, E1 enzyme and DNMT3A mutations exhibit elevated rates of CHIP and MDS, respectively. Although this relationship is unknown, clonal cells with TET2 or DNMT3A mutations may have a proliferative advantage in the inflammatory microenvironment or contribute to it in order to influence the development of AML. Myeloid cell proliferation can be modulated by cell intrinsic inflammatory signals and repression of inflammation in AML may contribute to survival.[22]

Staging

In the past, the French-American-British system classified AML into eight subtypes, FAB M0 to M7, which are as follows[15]:

- M0: Undifferentiated AML
- M1: AML with minimal maturation
- M2: AML with maturation
- M3: Acute promyelocytic leukemia (APL)
- M4: Acute myelomonocytic leukemia
- M5: Acute monocytic leukemia
- M6: Acute erythroid leukemia
- M7: Acute megakaryocytic leukemia

The newer WHO classification is based on molecular markers and morphology.

WHO classification of acute myeloid leukemia. AML and related neoplasms:

- AML with recurrent genetic abnormalities
- AML with t(8;21)(q22;q22.1); RUNX1-RUNX1T1
- AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11
- APL with PML-RARA
- AML with t(9;11)(p21.3;q23.3);MLLT3-KMT2A
- AML with t(6;9)(p23;q34.1);DEK-NUP214
- AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2, MECOM
- AML (megakaryoblastic) with t(1;22)(p13.3;q13.3); RBM15-MKL1
- AML with mutated NPM1
- AML with biallelic mutations of CEBPA
- AML with myelodysplasia-related changes

Therapy-related myeloid neoplasms

- AML, NOS
- AML with minimal differentiation
- AML without maturation
- AML with maturation
- Acute myelomonocytic leukemia
- Acute monoblastic/monocytic leukemia
- Pure erythroid leukemia
- Acute megakaryoblastic leukemia
- Acute basophilic leukemia
- Acute panmyelosis with myelofibrosis
- Myeloid sarcoma

- Myeloid proliferations related to down syndrome
- TAM
- Myeloid leukemia associated with down syndrome

Treatment / Management

Complete remission (CR) is associated with an increased prognosis in patients who undergo induction therapy and attain a blast count in the bone marrow of less than 5%. Notwithstanding the implementation of induction therapy, residual disease remains to a negligible extent. In order to mitigate the risk of relapse, consolidation therapy is initiated to eradicate the residual disease. Therapy continues to be predicated on a combination of anthracycline-based and cytarabine-based regimens, despite numerous advancements. Consideration should be given to allogeneic stem cell transplantation for eligible candidates.[23,24]

Induction Therapy

This is the prevailing approach for managing younger patients, geriatric individuals with favorable and intermediate-risk factors, and those with a low risk of treatment-related mortality (TRM). The induction therapy induces severe toxicity in the bone marrow, resulting in complications such as gastrointestinal system disturbances, kidney failure due to tumor lysis syndrome, electrolyte imbalances and pancytopenias and hemorrhage. Cell counts recovery could take up to one month and these patients require vigilant monitoring to prevent complications. Prior to commencing treatment, it is imperative to assess baseline cardiac function and closely monitor the ejection fraction (EF), given that anthracyclines have the potential to induce substantial cardiotoxicity. The treatment consists of the "7+3" regimen, which comprises of anthracycline on days one through three and a continuous infusion of cytarabine for seven days. Patients diagnosed with refractory disease who received higher doses of cytarabine or a combination of fludarabine, cytarabine and idarubicin exhibited comparable overall survival (OS) and improved CR. Reinduction may be achieved through the combination of etoposide and high-dose

cytarabine, provided that disease manifestations persist. 60% to 80% of de novo AML patients who receive induction therapy achieve CR.[15]

Consolidation Therapy

Once complete remission (CR) has been achieved through induction therapy, consolidation therapy is initiated using hematopoietic cell transplantation (HCT) and high dose cytarabine (HiDAC). HCT is the treatment of choice for patients with intermediate or unfavorable prognoses who are younger than 60 years old. In the presence of a donor, allogeneic HCT is favored over autologous HCT. Symptoms or indications of acute or chronic graft versus host disease (GVHD) should prompt their monitoring.

Prognosis

Clinicians can determine whether standard therapy or more intensive therapy would be more beneficial in sustaining CR and OS rates by evaluating prognostic factors. Chromosome abnormalities (t(8;21), t(15;17), inversion of chromosome 16, and genetic mutations (NPM1 gene has an advantageous prognosis, whereas FLT3 gene has an unfavorable prognosis) are prognostic factors. Age, a white blood cell count exceeding 100,000 at the time of diagnosis, s-AML, t-AML and the presence of leukemic cells in the central nervous system have all been associated with unfavorable outcomes. In patients with CR, contemporary methods including PCR and flow cytometry can identify the existence of minimal residual disease. In patients with t(8;21) AML, persistently elevated levels of RUNX1-RUNX1T1 despite induction therapy are associated with an increased risk of relapse.

Zaki S et al.[25] (2002) assessed the treatment and clinical characteristics of pediatric patients with acute myeloid leukemia. Retrospective analysis of hospitalized minors (less than 14 years) diagnosed with AML using chart-based data. Twenty-three patients were admitted in total. The average age was 8 years and 5 months. The most prevalent morphological subtype was M3 (43%). A total of 92 percent of

the patients exhibited hyperleucocytosis (TLC > 100 x 10(9)/L), while 95% displayed an increased LDH level (> 548 IU/L). Pneumonia was observed in 29% of cases at presentation. Out of a total of 23 patients, 14 were available for evaluation of responses. There were six premature deaths (43 percent), three prior to the initiation of chemotherapy and three during induction; eight out of eleven patients (73 percent) achieved remission. Survival times were nine months on average. Acute myeloid leukemia in children, to conclude, is characterized by the presence of advanced disease. Early mortality is prevalent (within 28 days of diagnosis). The long-term results were not as favorable as those documented in the scientific literature.

The hematologic and immunophenotypic profile of 260 cases of acute myeloid leukemia at the time of diagnosis was evaluated by Ghosh S et al.[10] in 2003. A retrospective analysis of 260 cases of AML was conducted. The diagnosis was established through the analysis of peripheral blood and bone marrow for immunophenotypic, cytochemical and morphological purposes. AML-M2 was the most prevalent subtype of FAB in both adolescents and adults. Antimyloid-M1 exhibited the highest WBC counts, while AML-M3 displayed the lowest. Hemoglobin levels averaged 6.8 gm/l (1.8 gm/l to 9.2 gm/l), platelet count was 63.3 x 10(9)/L, peripheral blood blasts comprised 41.4%, and bone marrow blasts constituted 57.6%. Positive myeloperoxidase levels were greatest in subtypes M1, M2, and M3. In diagnosing AML, CD13 and CD33 emerged as the most valuable biomarkers. Most frequently observed in monocytic and myelomonocytic leukemia were CD14 and CD36. In 15% of the cases, lymphoid antigen expression was detected. Expression of CD7 was most prevalent. In summary, AML comprised 39.8% of the total number of leukemia identified. Adults comprised 76% of the patient population. AML, subtype M2, was the most prevalent in both infants and adults. In diagnosing AML, CD13 and CD33 emerged as the most valuable biomarkers. 15% of the cases exhibited aberrant lymphoid

expression, with CD7 being the lymphoid marker that was most frequently expressed.

Saikia TK et al.[26] (2005) examined the prognosis of AML in a cohort of single-center-treated patients (15–60 years of age). 15–60 years of age and newly diagnosed with AML (excluding acute promyelocytic leukemia), 166 patients were administered induction chemotherapy consisting of daunorubicin or idarubicin in combination with cytarabine. Two cycles of high-dose cytarabine were administered after remission, followed by four cycles of outpatient maintenance chemotherapy administered monthly, which consisted of daunorubicin. Six patients in remission were administered allogeneic HSCT from a sibling donor. Complete morphological remission was observed in 69.9% of the patients. A prevalence of resistant disease was observed in 14.6% of patients following induction chemotherapy, with early mortality affecting 16%. Relapse-free survival was observed to be 22%, while event-free survival accounted for 34% over a median of 36 months. The relapse rate was 43.9%. The research findings indicate that a 3+7 regimen, comprising a higher dose of daunorubicin and two cycles of HiDAC, results in a favorable remission rate of two-thirds and extended-functioning status in one-third of patients diagnosed with AML in adults.

In 2009, Cheng Y et al.[27] investigated the karyotypic patterns of 1432 de novo AML patients from a single Centre in China. The authors also conducted a comparative analysis of their data with reports from other global regions. The presence of chromosomal abnormalities was identified in 746 cases or 58%. In 14% of successful cases, the t(15;17) cytogenetic abnormality was identified as the most prevalent. This was followed by the t(8;21) at 8% and the t(9;22), +21, and +8 at 2% each. Patients with a translocation karyotype had a substantially younger mean age than those with deletion, trisomy, or normal karyotypes. The Asian population exhibited a greater prevalence of AML M3 and a reduced

occurrence of M4. Additionally, the frequencies of specific cytogenetic aberrations differed from those documented in previous studies.

Critically ill AML patient's clinical characteristics and outcomes were described by Roze des Ordons AL et al.[28] in 2010**.** Cases in a retrospective case-control study were defined as intensive care unit-admitted adult patients with a primary diagnosis of AML. Age, gender, and illness severity (ICU only) were utilized to match each case with one of two control groups: hospitalised AML controls or non-AML ICU controls. Sepsis and respiratory failure were the principle diagnoses. SOFA score 12.6 (mean (standard deviation): APACHE II score was 30.3; 62.2% were undergoing mechanical ventilation, 55.6% vasoactive therapy and 26.7% renal replacement therapy. The respective crude in-hospital, 90-day and one-year mortality rates were 44.4%, 51.1% and 71.1%. The adjusted-hazards of mortality for AML patients were considerably greater in comparison to both non-AML ICU controls and hospitalized AML controls. Older age, subtype of acute myeloid leukemia, higher baseline SOFA score, no change or an increase in early SOFA score, shock, vasoactive therapy and mechanical ventilation were all factors associated with ICU mortality according to univariate analysis. In summary, although AML patients may constitute a small proportion of all critically ill admissions, they are frequently assisted in the intensive care unit. The mortality risk of these AML patients is greater than that of matched hospitalized AML or non-AML ICU controls, due to their severe illness, multi-organ dysfunction, and intensive treatment.

In 2012, Venkateswaran SP et al.[5] investigated the clinicopathological correlation between acute lymphoblastic and acute myeloid leukemia using cytogenetics and immunophenotyping. This investigation encompassed all cases of acute myeloid leukemia that were recently diagnosed. Using the French-American-British (FAB) Cooperative Group Classification, surface membrane, cytoplasmic, and nuclear antigens in the bone marrow and peripheral blood were analyzed. In acute

myeloid and lymphoblastic leukemia, immunophenotype-based antigen expressions were compared to platelet counts, lactate dehydrogenase levels, age, hemoglobin, total white blood cell count, and anomalous karyotypes. There was a significant correlation between the expressions of CD13, CD33, CD117, and CD64 in Acute Myeloid Leukemia and CD10, CD19, CD20, and CD22 in Acute Lymphoblastic Leukemia, as determined by analytical statistics. Age, hemoglobin, white blood cell count, and lactate dehydrogenase levels were found to be associated with the expressions of CD117/CD117, CD3/CD10/CD22, CD3/CD5/CD2, and CD117/CD11c, respectively. In summary, the research identified a statistically significant correlation among several parameters and provided support for the notion that abnormal karyotypes and the expression of particular antigens are associated with an unfavorable prognosis in acute leukemias.

Fadoo Z et al.[29] documented the demographics and prognosis of children treated at a tertiary care facility for Acute Myeloid Leukemia (AML) in 2012. A retrospective analysis of adolescents (less than 15 years) diagnosed with AML was performed. In 83% of cases, fever was the predominant presenting feature, followed by pallor (39%), hemorrhage (41%) and fever (41%). Initial WBC counts exceeding 100,000 were observed in 19% of the patients. M4 was the most prevalent subtype of FAB at 39%. Twelve of the twenty-three patients who received treatment are currently alive and in a state of remission. The average duration of follow-up was 2 years and 6 months. Three of the eleven deceased patients had disease resistance, four relapsed and the remaining patients perished primarily from sepsis that developed during induction. In conclusion, AML M4 was the most prevalent subtype in this investigation, whereas AML M2 was reported to be the predominant subtype. A third of the patients encountered financial limitations that prevented them from initiating or finishing therapy. A total of 52% of our patients who successfully completed therapy survived.

In their study, Gmidene A et al.[30] (2012) attempted to ascertain the prevalence and subtypes of chromosomal abnormalities among patients with acute myeloid leukemia (AML) in the Tunisian population. Additionally, they seek to compare the cytogenetic profile of this population with previously published data from different geographical areas. By employing conventional cytogenetic, 631 newly diagnosed AML patients were examined in succession. The presence of aberrant karyotypes was identified in 397 (62.9%) of the total cases. The most prevalent chromosomal abnormalities identified in 83 patients (13.2%) and 78 patients (12.4%), respectively, were t(15;17) and t(8;21) –5/del(5q) and -7/del(7q) occurred in a reduced number of instances, specifically 14 (2.2%) and 19 (3%) cases, respectively. Trisomy 8 was identified in 44 patients (7 percent), 11q23 rearrangements were detected in 24 (3.8 percent) and inv(16) was detected in a mere 22 (3.5 percent) of the total cases. A total of 107 patients (17%) exhibited cytogenetic abnormalities that were deemed unusual or novel. The results of the research were more consistent with those observed in Eastern nations as opposed to those documented in Western societies.

Ayesh MH et al.[31] published the cytogenetic and morphological characteristics of de novo AML in adult Jordanian Arabs in 2012 with the intention of comparing the findings to those of comparable ethnic Arab populations worldwide. Patients who have been diagnosed with de novo AML in accordance with the French-American-British (FAB) criteria. Metaphases were absent in four patients due to hypo cellular bone marrow. M5 (55 percent) was the most prevalent morphological subtype, followed by M3 (19 percent). Twenty patients (65%) exhibited cytogenetic abnormalities; six patients (19%) had t(15;17) translocations, four patients (13%) had inv(16) translocations, two patients (4%), and none had t(8;21) translocations. The most prevalent numerical chromosomal abnormality was trisomy 8, which affected four patients (13%). There were both distinctions and parallels with Arab populations of similar ethnic

background. Among chromosomal abnormalities, inversion (16), +8, and t(15;17) were the most prevalent. Conclusion: Age, gender, morphologic subtype, and chromosomal abnormalities exhibited both similarities and differences among ethnic Arabs in Jordan who were diagnosed with de novo AML.

Pouls RK et al.[32] (2012) assessed adult AML patients' clinical and hematological parameters. A meticulous examination of the medical records of 94 adult patients diagnosed with acute myeloid leukemia was conducted. Evaluation of peripheral blood and bone marrow provided the diagnosis. Cytochemistry was utilized to validate the myeloid lineage, and morphological subtyping was performed in accordance with the French-American-British (FAB) criteria. The most prevalent initial manifestation was pallor (70.2%), which was succeeded by hemorrhage (22.3%) and fever (7.5%). The average Hb level was 7.6 g/dL, while the WBC and platelet counts were 34.5x10-6/L and 39.6x10-9/L, respectively. Blast cell percentages were 42.5% in the peripheral blood and 65.9% in the bone marrow. At 24.4%, AML-M2 was the most prevalent subtype of FAB. In summary, AML was more prevalent among males compared to females. AML-M2 was the most prevalent subtype of FAB. Pallor was the most frequently observed presenting characteristic. Utilizing Sudan black-B stain to diagnose myeloid leukemia proved to be an effective procedure.

Sultan S et al.[33] identified the current spectrum of subtypes of AML in patients in 2016. A single centre cross-sectional investigation was conducted. De novo AML was identified in 125 patients, of which 76 were male and 49 were female. The most prevalent subtype of FAB (23.2%) was AML-M1, which was followed by M2, M3, M4, M0, M5, M6, and M7. In conclusion, AML is observed in a comparatively youthful population of Pakistani patients. The subtype of FAB that was most frequently identified in this research was acute myeloblastic leukemia, non-maturitating (M1).

Jacob S et al.[34] evaluated the clinico pathological characteristics and short-term prognosis of adult patients with AML in 2019. All patients

who were at least 18 years of age were enrolled. As induction chemotherapy, 100 mg/m2 of cytarabine was infused daily for seven days, and 60 mg/m2 of daunorubicin was administered daily for three days; three cycles of high-dose cytarabine were administered as post-remission therapy. In total, 102 patients were enrolled in the research. 13 patients succumbed to their conditions prior to undergoing chemotherapy, while 71 patients (57 of whom did not have AML M3) were administered induction chemotherapy. An Eastern Cooperative Oncology Group performance score of no less than 2 was achieved by 82% of the patients. Out of 57 non-AML M3 patients, 28 survived postremission therapy and 15 of them remained in remission after a median follow-up period of nine months. Upon completion of the research, the event-free survival rate amounted to 22% (16 out of 71). In total, 63 patients out of 84 had passed away. Although sepsis was identified as the underlying cause of death in 46% of the patients, only a minority (20%) were able to isolate the causative organism. In conclusion, AML treatment outcomes were unsatisfactory.

In their study, Shoket et al.[7] (2019) examined the clinical characteristics of acute myeloid leukemia (AML), the distinction between patients with the M3 phenotype and those without, and the influence of various factors on survival. The patients who were enlisted in the study underwent examination, evaluation and were administered the standard 3:7 induction protocol. In the case of acute promyelocytic leukemia (APML), the ICAPL 2006 protocol was utilized. The study unveiled that individuals in their twentieth year of life exhibited the most favorable prognosis. The platelet and total leukocyte counts had a substantial effect on the patient's survival. The bone marrow morphology of type M3 has the highest prognosis and was the most prevalent FAB type observed in our research. Positive flow cytometric markers included myeloperoxidase, CD15, CD33, and CD117, which were detected in 90% of the patients. Survival rates for the entire study group are approximately 40%, the APML group 87%, and the non-M3 group 16.5%. Non-M3 patients continue to

face unfulfilled management requirements in resource-constrained nations with limited access to newer pharmaceuticals and allogenic transplants. Further experimental trials are utilizing more recent molecules, including PIK3 and Flt3 inhibitors, in an effort to improve the prognosis for M3 AML. In conclusion, non-M3 patient management in resource-constrained nations with limited access to newer medications and allogenic transplants remains unsatisfied. Further experimental trials are utilizing more recent molecules, including PIK3 and Flt3 inhibitors, in an effort to improve the prognosis for M3 AML.

Elnaggar MG et al.[35] evaluated the cytogenetic characteristics of adult AML patients in southern Egypt in 2022. Chryotyping and M-FISH cytogenetic analyses were conducted on 120 adult patients diagnosed with AML. Twenty metaphases per patient were analyzed. AML patients ranged in age from 18 to 86 years, with a median age of 36.5 years. 43.3% of patients had clonal cytogenetic abnormalities, while 56.7% of patients had normal karyotypes. +8 was the most frequently detected numerical anomaly, while t (15;17) was the most frequently detected structural anomaly. In terms of cytogenetic risk stratification, the intermediate-risk category comprised 65% of the patients. In summary, the cytogenetic characteristics of acute myeloid leukemia (AML) patients in their specific geographic region exhibited both distinctions and parallels with cytogenetic profiles from various Arab, Asian, and Western nations. Utilizing cutting-edge methodologies like next-generation sequencing and optical genome mapping, additional research is required to elucidate the ethnic and geographical genetic heterogeneity that exists between nations.

MATERIAL AND METHODS

SOURCE OF DATA

All the patients aged more than 18 years admitted with acute myeloid leukemia in Department of Medicine and allied Specialties of Dayanand Medical College and Hospital (DMCH), Ludhiana

METHOD OF COLLECTION OF DATA

Study Population

A prospective observational study was conducted in adults patients admitted with acute myeloid leukemia in DMCH, Ludhiana. The study duration was from 1st October 2022 to 31st March 2024.

Inclusion Criteria

- Age $\geq$ 18 years.
- Diagnosed cases of acute myeloid leukemia admitted in department of Medicine and allied Specialties

Exclusion Criteria

- Age < 18 years.
- Patients not giving consent for enrollment in the study.

OUTCOME

- Length of stay in hospital.
- Clinical/laboratory/treatment profile of admitted patients.
- Details of pre admission workup and treatment outside (wherever available)
- Documentation of complete hematologic remission and bone marrow remission after induction on bone marrow
- Outcome of the treatment and the type of treatment received (standard treatment or supportive care)
- Follow-up post-discharge (wherever feasible) at 3 months

Statistical Analysis:

The data was analyzed statistically using appropriate methodology. Data was described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies

(percentages) as appropriate. For comparing categorial data chi square test was used. To calculate survival probability Kaplan-Meier curve was ploted. The p values of <=0.05 was taken as significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science) 26 SPSS statistical program for Microsoft Windows.

DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Investigations considered necessary by the treating unit/department was evaluated. The investigations were broadly divided into the following groups:

- Basic investigations: CBC, LFT, RFT, Urine routine, inflammatory markers like ESR, LDH, CRP and/or any other
- Specific investigations:
    - Bone marrow aspiration and biopsy for morphology, cytochemistry, flow cytometry and cytogenetics by conventional karyotyping and/or any other technique
    - Molecular analysis using a targeted allele specific PCR or next generation sequencing for myeloid mutations (as feasible)
- Radiological investigations: Chest radiograph, US, CT Scan, MRI and/or PET scan
- Detailed proforma format is attached herewith with thesis plan

OBSERVATION AND RESULTS

The present prospective observational study was conducted in adult patients admitted with acute myeloid leukemia in medicine and allied specialities, from 1st October 2022 to 31st March 2024. The results of the study are discussed below

Table 1: Distribution of patients with AML with respect to Age

Age (years)	No. of patients		Percent	
<=20	1		2	
21-30	6		12	
31-40	7		14	
41-50	6		12	
51-60	10		20	
>60	20		40	
Total	50		100	
	Median	Percentiles		
		25	50	75
Age	54.00	37.00	54.00	66.00

Table 1 shows the distribution of patients according to age. The distribution indicates that the majority of AML patients are older, with 40% being over 60 years old and 20% being in the 51-60 years age group. The median age of the patient was54 years (IQR=37-66).

Figure 1: Pie chart depicts the Age distribution of patients with AML

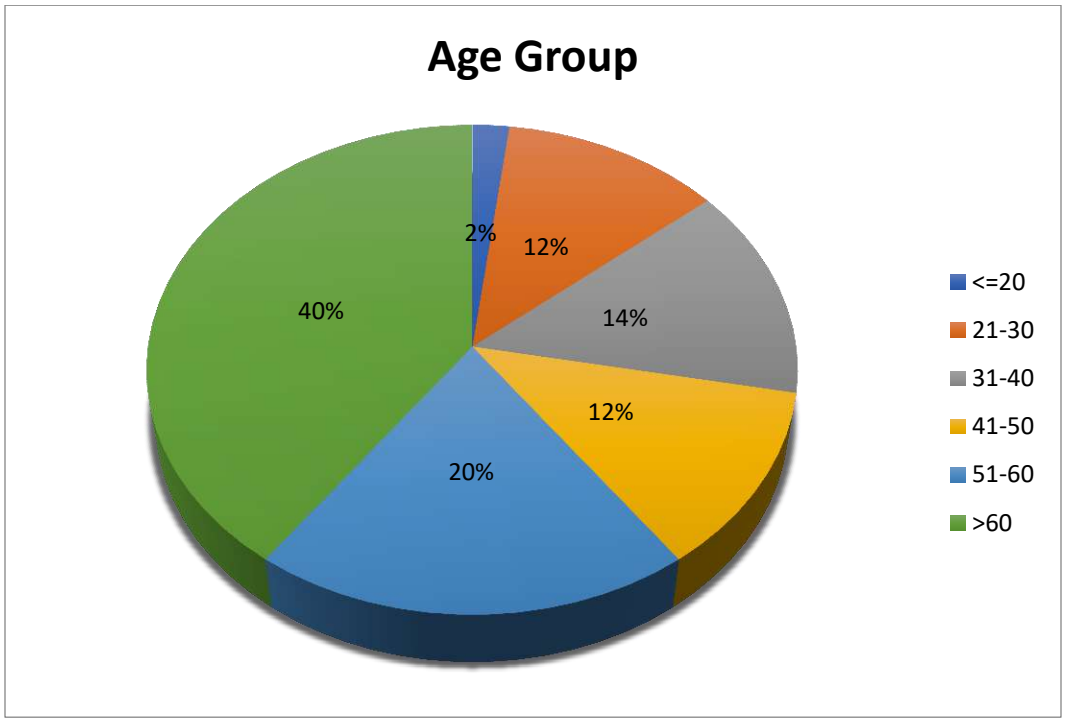


Table 2: Distribution of patients with AML with respect to gender

Gender	No. of patients	Percent
Female	24	48
Male	26	52
Total	50	100

The majority of the patients were males constituting 52% and females constituting 48%.

Figure 2: Pie chart depicts the Gender distribution of patients with AML

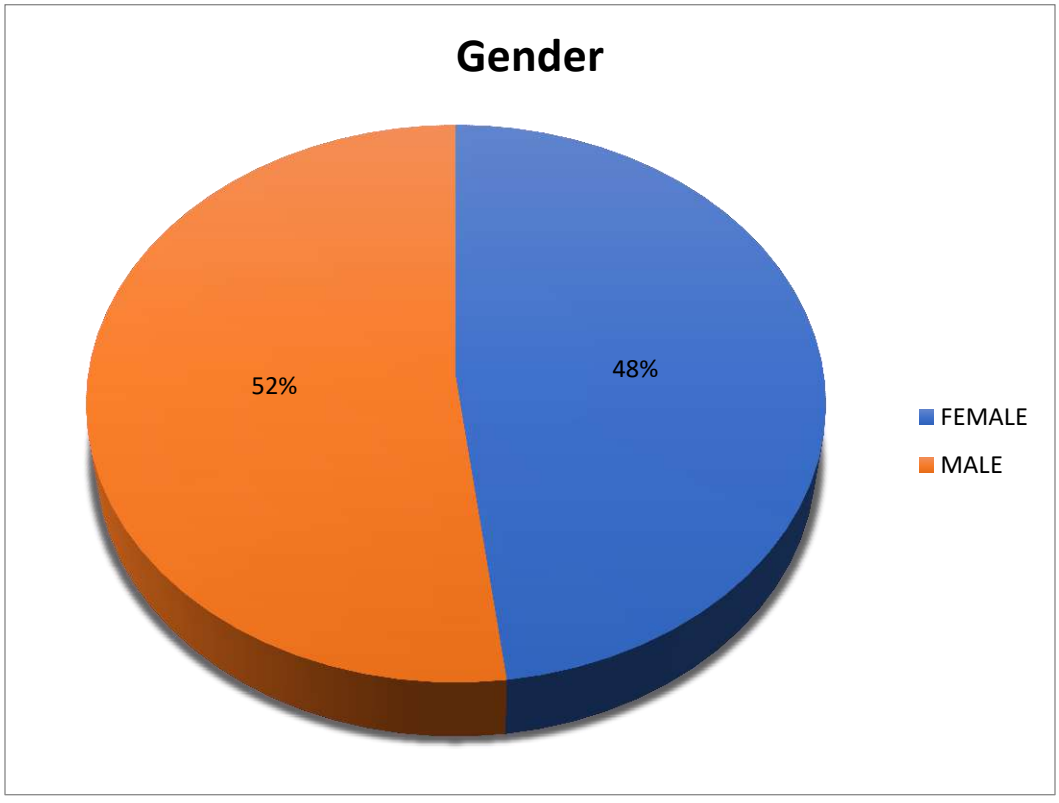


Table 3: Distribution of patients with AML with respect to Chief complaint

Chief complaints	No. of patients	Percent
Fever	40	80
Generalized weakness	24	48
Cough	15	30
Bleeding manifestation	9	18
Shortness of breath	7	14
Altered sensorium	1	2

Table 3 presented the distribution of chief complaints among patients with acute myeloid leukemia (AML). Fever was the most common chief complaint (80%), followed by generalized weakness (48%), cough (30%), bleeding manifestation (18%), shortness of breath (14%), and altered sensorium (2%). These findings highlighted that fever and generalized weakness were the most prevalent symptoms among AML patients in the study.

Figure 3: Bar diagram depicting the distribution of patients with AML with respect to the Chief complaints

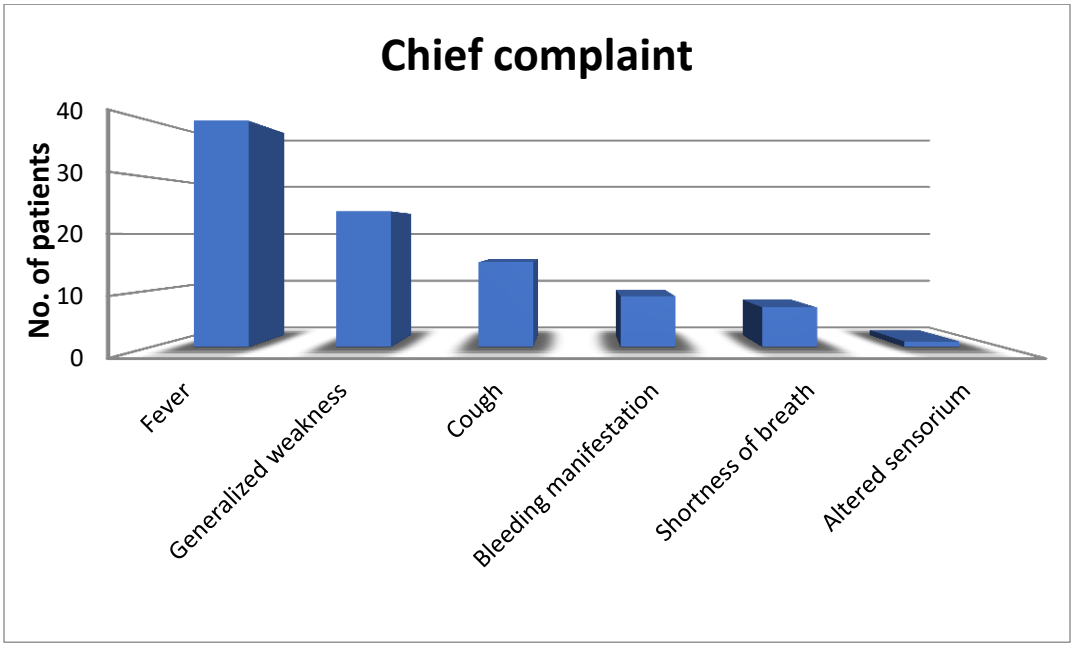


Table 4: Distribution of patients with AML with respect to Bleeding manifestations

Bleeding manifestation	No. of patients	Percent
Not present	41	82
Gum bleeding	2	4
ICH	2	4
Lower GI bleed	1	2
Melena	1	2
Menorrhagia	1	2
Subdural hematoma	1	2
Nasal bleeding	1	2
Total	50	100

The table summarizes bleeding manifestations among 50 patients, of which 18% reported various types of bleeding, each affecting a small portion of the sample: gum bleeding and intracerebral hemorrhage (4% each), and lower gastrointestinal bleed, melena, menorrhagia, subdural hematoma, and nasal bleeding (2% each). This indicates that while most individuals did not have bleeding issues, a few experienced diverse and serious types of bleeding.

Figure 4: Bar chart depicting the distribution of patients with AML with respect to bleeding manifestations

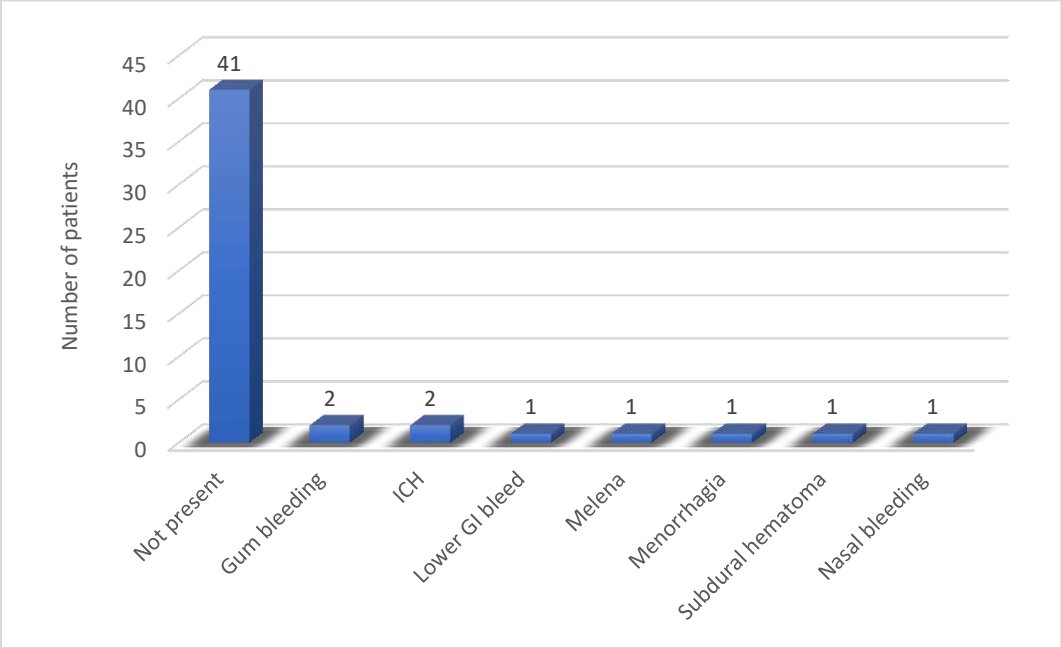


Table 5: Distribution of patients with AML with respect to General and systemic examination

Examination			No. of patients	Percentage
General Examination		Pallor	26	52
		Icterus	1	2
Systemic Examination	CNS	Decreased GCS	2	4
		Normal	48	96
	Abdomen	Normal	39	78
		Hepatomegaly plus splenomegaly	11	22

Table 5 shows the general and systemic examination findings for patients with acute myeloid leukemia (AML). In the general examination, pallor was a common finding, present in 52% of the patients, while icterus was rare, seen in only 4%. Systemic examination, In central nervous system (CNS) status, 96% of patients had normal findings, whereas 2% exhibited a decreased Glasgow Coma Scale (GCS). Abdominal examination results showed that 78% of patients had normal findings, while 22% had hepatomegaly and splenomegaly.

Figure 5: Bar chart showing the distribution of patients with AML with respect to General and systemic examination

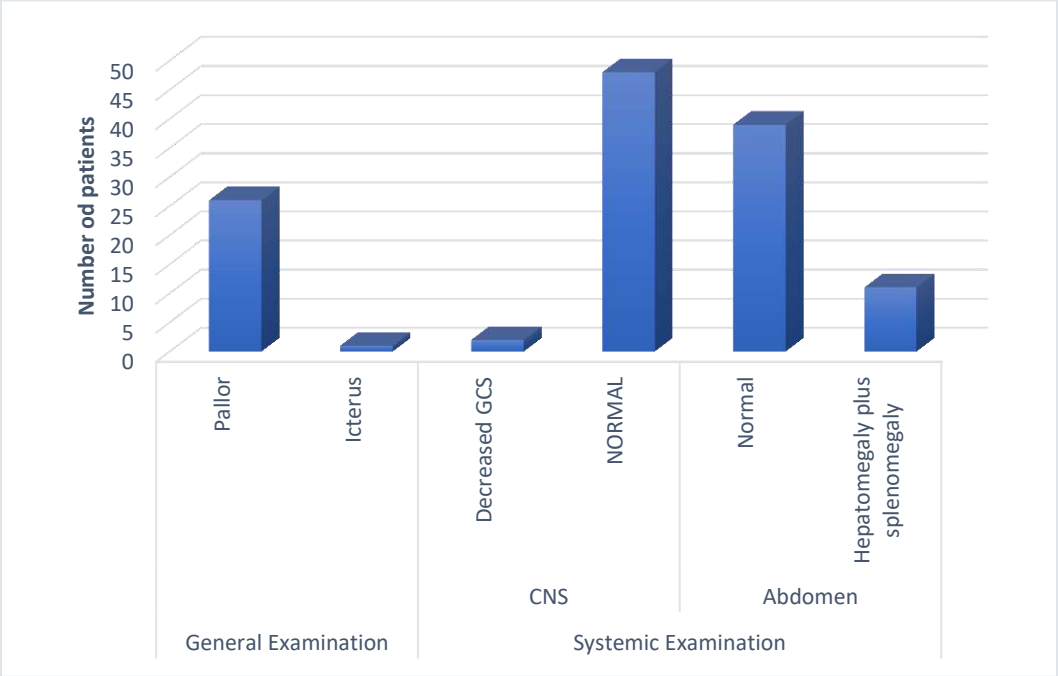


Table 6: Showing the grouped data for routine investigations performed.

	Median	Percentiles		
		25	50	75
AGE	54.00	37.00	54.00	66.00
TLC	22.45	2.73	22.45	48.05
HB	7.00	5.58	7.00	8.33
PLATELET	40.00	16.00	40.00	72.50
PTI	15.20	14.10	15.20	17.20
INR	1.33	1.25	1.33	1.51
BIL (t)	0.59	0.47	0.59	0.82
BIL(d)	0.17	0.10	0.17	0.33
SGOT	24.50	15.50	24.50	40.75
SGPT	23.50	16.00	23.50	44.25
ALP	78.00	60.00	78.00	108.00
CREATININE	0.86	0.71	0.86	1.13
Na	136.00	134.00	136.00	138.25
K	4.09	3.80	4.09	4.40
Cl	102.00	99.00	102.00	105.00
Calcium	8.30	8.00	8.30	9.20
MAGNESIUM	2.55	1.96	2.55	2.78
PHOSPHORUS	2.35	1.92	2.35	2.95

- **AGE**: Median age is 54 years with an interquartile range (IQR) from 37 to 66 years.
- **TLC (Total Leukocyte Count)**: The median TLC is 22.45, with a 25th percentile of 2.73 and a 75th percentile of 48.05.
- **HB (Hemoglobin)**: Median hemoglobin level is 7.00, with an IQR from 5.58 to 8.33.

- **PLATELET**: The median platelet count is 40.00, with a 25th percentile of 16.00 and a 75th percentile of 72.50.
- **PTI (Prothrombin Time Index)**: The median PTI is 15.20, with an IQR from 14.10 to 17.20.
- **INR (International Normalized Ratio)**: Median INR is 1.33, with a range from 1.25 to 1.51.
- **BIL (t) (Total Bilirubin)**: The median total bilirubin is 0.59, with an IQR from 0.47 to 0.82.
- **BIL (d) (Direct Bilirubin)**: Median direct bilirubin is 0.17, with an IQR from 0.10 to 0.33.
- **SGOT (Serum Glutamic-Oxaloacetic Transaminase)**: The median SGOT is 24.50, with an IQR from 15.50 to 40.75.
- **SGPT (Serum Glutamic-Pyruvic Transaminase)**: The median SGPT is 23.50, with an IQR from 16.00 to 44.25.
- **ALP (Alkaline Phosphatase)**: Median ALP is 78.00, with an IQR from 60.00 to 108.00.
- **CREATININE**: The median creatinine level is 0.86, with an IQR from 0.71 to 1.13.
- **Na (Sodium)**: Median sodium level is 136.00, with an IQR from 134.00 to 138.25.
- **K (Potassium)**: The median potassium level is 4.09, with an IQR from 3.80 to 4.40.
- **Cl (Chloride)**: Median chloride level is 102.00, with an IQR from 99.00 to 105.00.
- **Calcium**: The median calcium level is 8.30, with an IQR from 8.00 to 9.20.
- **MAGNESIUM**: The median magnesium level is 2.55, with an IQR from 1.96 to 2.78.
- **PHOSPHORUS**: The median phosphorus level is 2.35, with an IQR from 1.92 to 2.95.

Table 7: Distribution of patients with AML with respect to changes in HRCT chest during course of treatment.

HRCT Chest	No. of patients	Percent
Not done	20	40
Superadded Infection (probable bacterial or viral infection)	17	34
Normal	5	10
Fungal infection	5	10
Pleural / Pericardial effusion	2	4
Fluid overload	1	2

The table shows the distribution of HRCT chest findings in patients with Acute Myeloid Leukemia (AML) during treatment. HRCT was not done for 40% of patients. Among those who had HRCT, the most common finding was superadded infection (probable bacterial or viral infection) (34%). Other findings included fungal infection (10%), no abnormalities (10%), pleural/pericardial effusion (4%), and fluid overload alone (2%). This indicates a variety of complications detected through HRCT in AML patients undergoing treatment.

Figure 6: Bar chart depicting the distribution of patients with AML with respect to changes in HRCT chest during the course of treatment

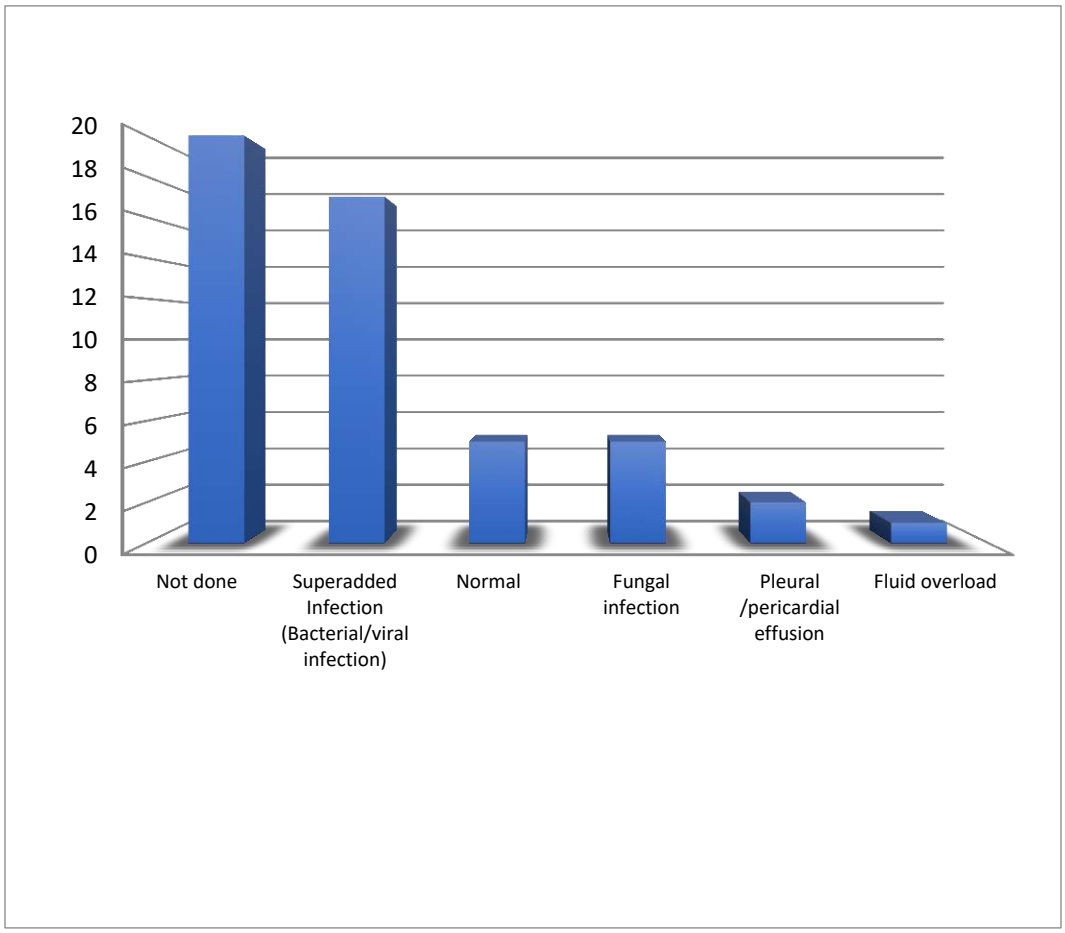


Table 8: Distribution of patients with AML with respect to Changes on 2D Echo.

2D Echo	No. of patients	Percent
Not done	9	18
Systolic dysfunction	2	4
Normal LVEF=60 %	39	78
Total	50	100

The table summarizes the 2D Echo results for 50 patients. 2D Echo was not performed in 18% of the patients. Among those who underwent the test, 4% had systolic dysfunction, while 78% had a normal Left Ventricular Ejection Fraction (LVEF) of 60%, indicating normal heart function.

Figure 7: Pie chart depicting the distribution of patients with AML with respect to Changes in 2D Echo

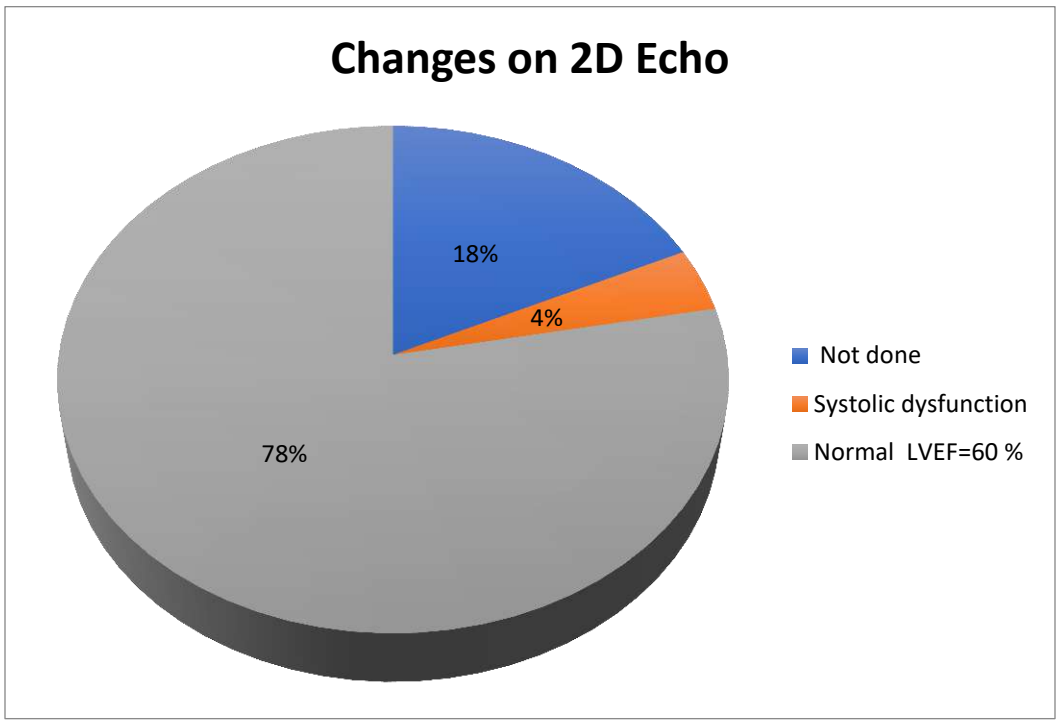


Table 9: Distribution of patients with respect to Flow cytometry analysis of patients.

CD markers	No. of patients	Percent
CD13	35	70.00
CD117	34	68.00
CD33	30	60.00
HLADR	27	54.00
CD38	27	54.00
CD34	20	40.00
CD123	18	36.00
MPO	16	32.00
CD64	10	20.00
CD14	4	8.00
CD11 b	3	6.00
CD10	2	4.00

Table 9 shows the flow cytometry analysis. The most commonly expressed markers were CD13 (70%), CD117 (68%), and CD33 (60%). HLADR and CD38 were each present in 54% of the patients. CD34 was found in 40%, while CD123 was present in 36% of the patients. MPO (myeloperoxidase) was noted in 32%, and CD64 in 20%. Less common markers included CD14 (8%), and CD11 b found in 6% of the patients. The least expressed markers were CD10 (4%).

Figure 8: Bar chart depicting the distribution of patients with AML with respect to flow cytometry analysis of patients

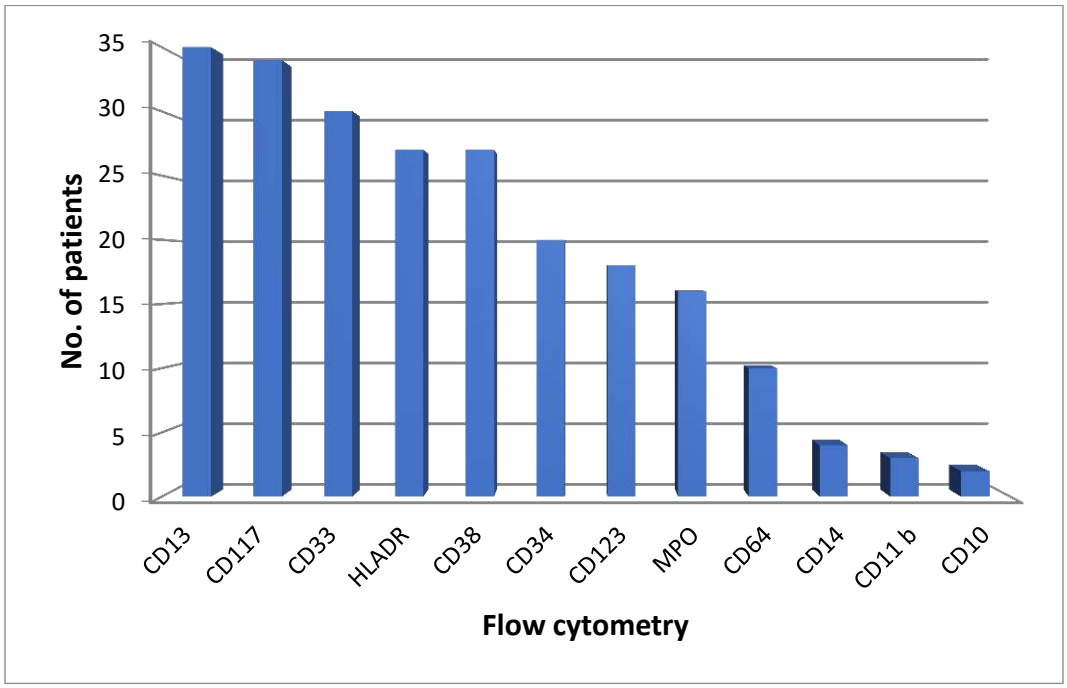


Table 10: Distribution of patients with respect to FAB grading of AML

Grades	No. of patients	Percent
M0/M1	8	16
M1	4	8
M2	14	28
M3	10	20
M4	12	24
M5	2	4
Total	50	100

The table shows the distribution of 50 AML patients by FAB classification. The most common subtypes are M2 (28%) and M4 (24%), followed by M3 (20%). Less frequent subtypes include M0/M1 (16%), M1 (8%), and M5 (4%). This indicates a higher prevalence of M2 and M4 among the patients.

Figure 9: Pie chart depicting the Distribution of patients with respect to grading of AML

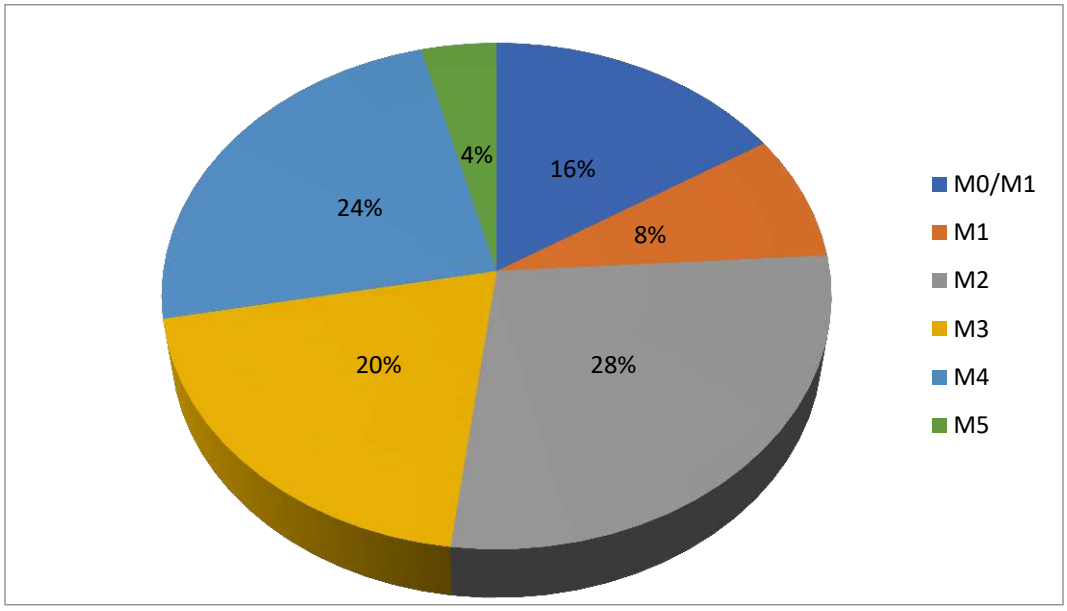


Table 11: Distribution of patients with respect to M3 and non-M3 AML

Grades	No. of patients	Percent
M3	10	20
Non M3	40	80
Total	50	100

The table provides the distribution of patients with Acute Myeloid Leukemia (AML) classified into M3 and non-M3 subtypes. Among the 50 patients, 20% were diagnosed with M3 AML, while the majority, 80%, were diagnosed with non- M3 AML. This indicates a higher prevalence of the M3 subtype within the studied group

Figure 10: Distribution of patients with respect to M3 and non-M3 AML

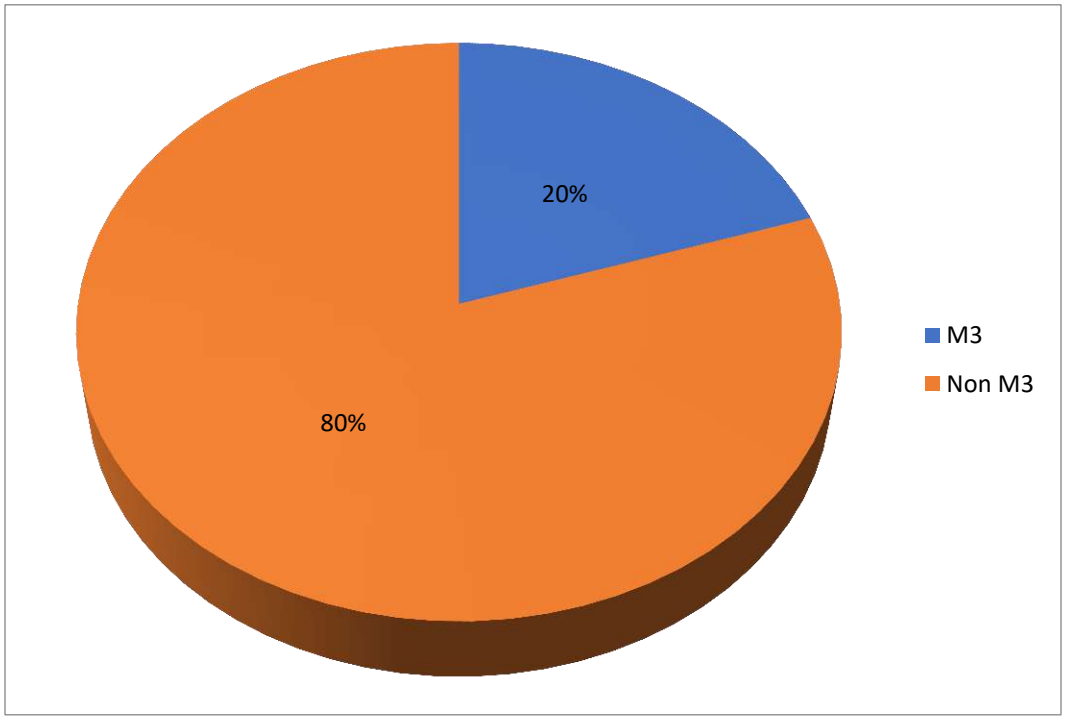


Table 12: Association of FAB grading of AML and flow cytometry

	Non M3		M3		Total		chi square	p-value
	n	%	n	%	n	%		
CD13	30.00	75.00	5.00	50.00	35.00	70.00	2.38	0.12
CD117	27.00	67.50	7.00	70.00	34.00	68.00	0.02	0.88
CD33	23.00	57.50	7.00	70.00	30.00	60.00	0.52	0.47
HLADR	26.00	65.00	1.00	10.00	27.00	54.00	9.74	0.00
CD38	22.00	55.00	5.00	50.00	27.00	54.00	0.08	0.78
CD34	17.00	42.50	3.00	30.00	20.00	40.00	0.52	0.47
CD 123	13.00	32.50	5.00	50.00	17.00	34.00	1.06	0.30
MPO	10.00	25.00	6.00	60.00	16.00	32.00	4.50	0.03
CD64	5.00	12.50	5.00	50.00	10.00	20.00	7.03	0.01
CD14	2.00	5.00	2.00	20.00	4.00	8.00	2.45	0.12
CD7	4.00	10.00	0.00	0.00	4.00	8.00	1.09	0.30
CD11b	2.00	5.00	1.00	10.00	3.00	6.00	0.36	0.55
CD10	2.00	5.00	0.00	0.00	2.00	4.00	0.52	0.47

1. HLADR: Significant association (p = 0.00), with higher expression in non-M3 cases (65%) compared to M3 cases (10%).
2. MPO: Significant association (p = 0.03), with higher expression in M3 cases (60%) compared to non-M3 cases (25%).
3. CD64: Significant association (p = 0.01), with higher expression in M3 cases (50%) compared to non-M3 cases (12.5%).

Markers such as CD13, CD34, and CD38 showed no significant association with either AML subtype, indicating similar expression patterns across non-M3 and M3 cases. The data highlights specific markers, particularly HLADR, MPO, and CD64, which could serve as potential diagnostic indicators differentiating between non-M3 and M3 AML

Figure 11: Association of FAB grading of AML and flow cytometry

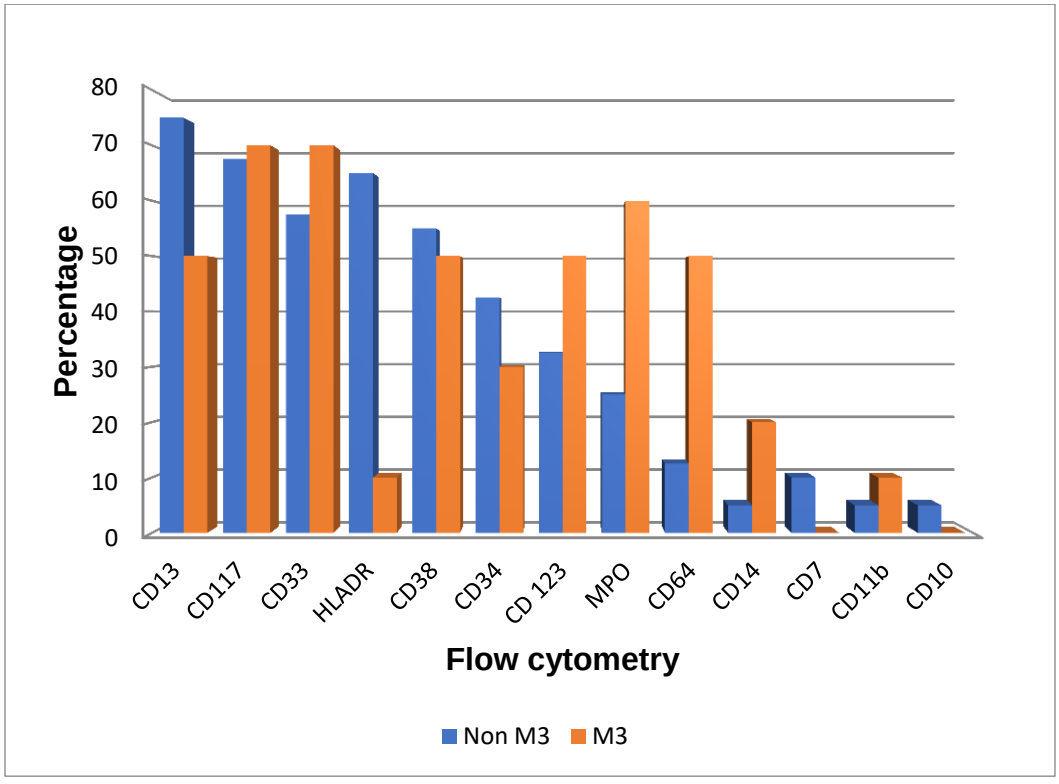


Table 13: Distribution of patients with respect to *RT-PCR* panel

		No. of patients	Percentage
RTPCR positive	NPM -1	8	16
	FLT3	2	4
	PML- RARA	4	8
	FLT3-D835	2	4
	FLT3-ITD	4	8
	CBFB-MYH11	3	6
RTPCR negative		7	14

RT-PCR panel was performed in 23(32%) patients with AML. While it was negative for 7 cases. And wasn't performed for 27 cases. About the distribution and prevalence of specific genetic mutations identified through RT-PCR in the study cohort, we found that NPM-1 is the most frequently detected marker, found in 16% of patients, while FLT3 and FLT3-D835 are the least common, each present in 4% of patients. PML-RARA and FLT3-ITD are found in 8% and 6% of patients, respectively.

Figure 12: Bar chart showing distribution of patients with respect to *RT-PCR* panel

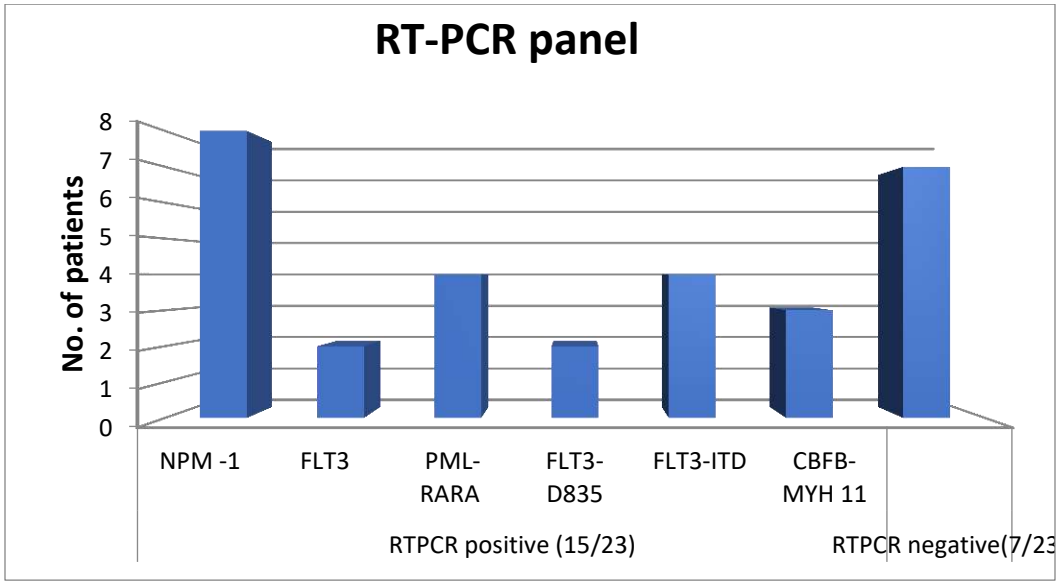


Table 14: Association of RT-PCR findings and FAB subtypes

		Non M3		M3	
	N=23 (%)	N	%	N	%
NPM -1	8(34%)	8	34	0	0
FLT3	2(8.6%)	2	8.6	0	0
PML-RARA	4(17%)	0	0	4	17
FLT3-D835	2(8.6%)	1	4.3	1	4.3
FLT3-ITD	3(13%)	1	4.3	2	8.6
CBFB-MYH 11	3(13%)	3	13	0	0

1. NPM-1: Detected in 34% of AML patients, with 34% cases in Non M3 and no case in M3 patients.
2. FLT3: Detected in 8.6% of AML patients, with 8.6% cases in Non M3 and no case in M3 patients.
3. PML-RARA: Detected in 17% of AML patients, with 17% cases in M3 and no case in Non M3 patients.
4. FLT3-D835: Found in 8.6 % of AML patients, with 4.3% cases in M3 patients and 4.3% cases in Non M3 patients.
5. FLT3-ITD: Detected in 13% of AML patients, with 4.3% cases in Non M3 and 8.6% cases in M3
6. CBFB-MYH11: Detected in 13% of AML patients, with 13% cases in Non M3 and no case in M3 patients.

This table shows that certain genetic markers, such as NPM-1, FLT3, and CBFB-MYH11, are present in non-M3 patients but absent in M3 patients. Conversely, PML-RARA and FLT3-ITD is more prevalent in M3 patients compared to non-M3 patients. These findings suggest distinct genetic profiles between the two subtypes, with some markers being subtype-specific

Figure 13: Association of RT-PCR findings and FAB subtypes

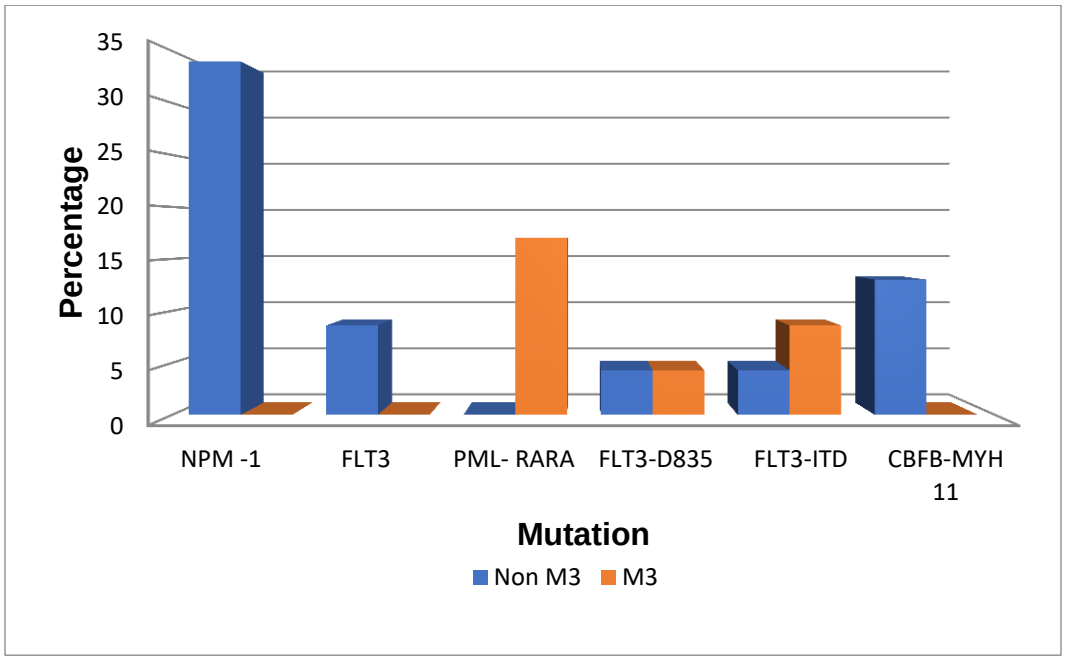


Table 15: Distribution of cases with AML according to the treatment given

	No. of patients	Percent
Hypomethylating Agents (Azacytidine, Decitabine)	11	22
Hypomethylating Agents (Azacytidine, Decitabine) with Venetoclax	16	32
Therapy not taken	9	18
ATO, ATRA and or mitoxantrone and or idarubicin	8	16
Daunorubicin plus cytarabine (7+3 regimen)	6	12
Total	50	100

This distribution shows that the majority of patients (54%) were treated with hypomethylating agents, either alone or in combination with Venetoclax. A significant proportion (18%) did not undergo any treatment, and the remaining patients were treated with either ATO, ATRA and/or mitoxantrone and/or idarubicin, or the daunorubicin plus cytarabine (7+3 regimen).

Figure 14: Pie chart depicting distribution of patients with respect to therapy undertaken by patients

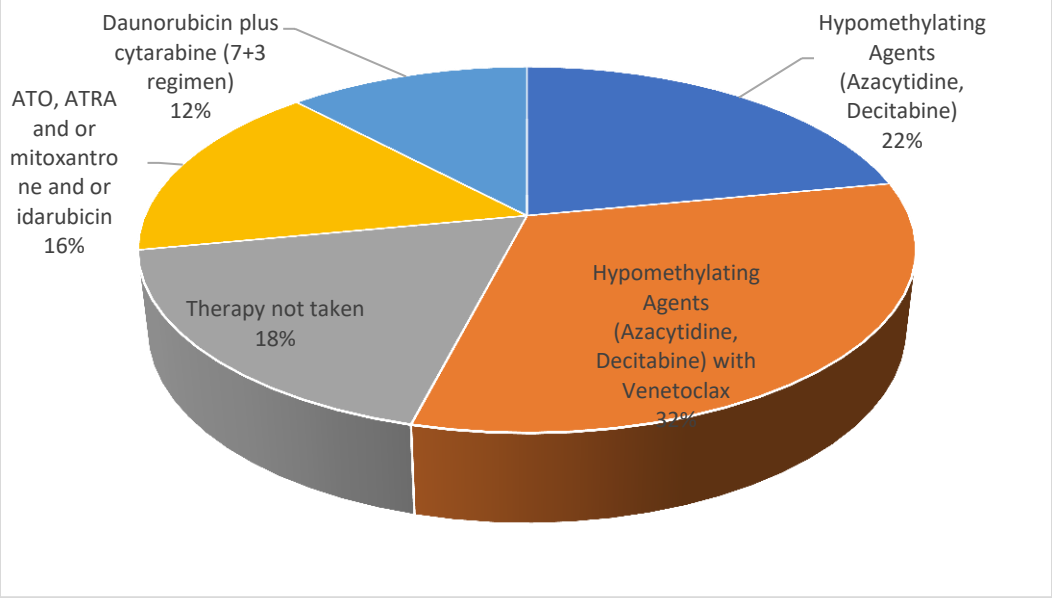

Daunorubicin plus cytarabine (7+3 regimen) 12%
Hypomethylating Agents (Azacytidine, Decitabine) 22%
ATO, ATRA and or mitoxantrone and or idarubicin 16%
Therapy not taken 18%
Hypomethylating Agents (Azacytidine, Decitabine) with Venetoclax 32%

Table 16: Distribution of patients with respect to time period for bone marrow remission

Bone marrow remission	No. of patients	Percent
≤ 30 days	9	18
31-60 days	3	6
>60 days	7	14
Total	19	38
Not done	31	62
Total	50	100

The table presents the distribution of patients with acute myeloid leukemia (AML) based on the time period required to achieve bone marrow remission. Among the 50 patients studied, 38% achieved bone marrow remission. Of these, 18% achieved remission within 30 days, 6% within 31-60 days, and 14% took more than 60 days. However, 62% of the patients did not give consent for again bone marrow test to check remission.

Figure 15: Bar chart depicting distribution of patients with respect to time period for bone marrow remission

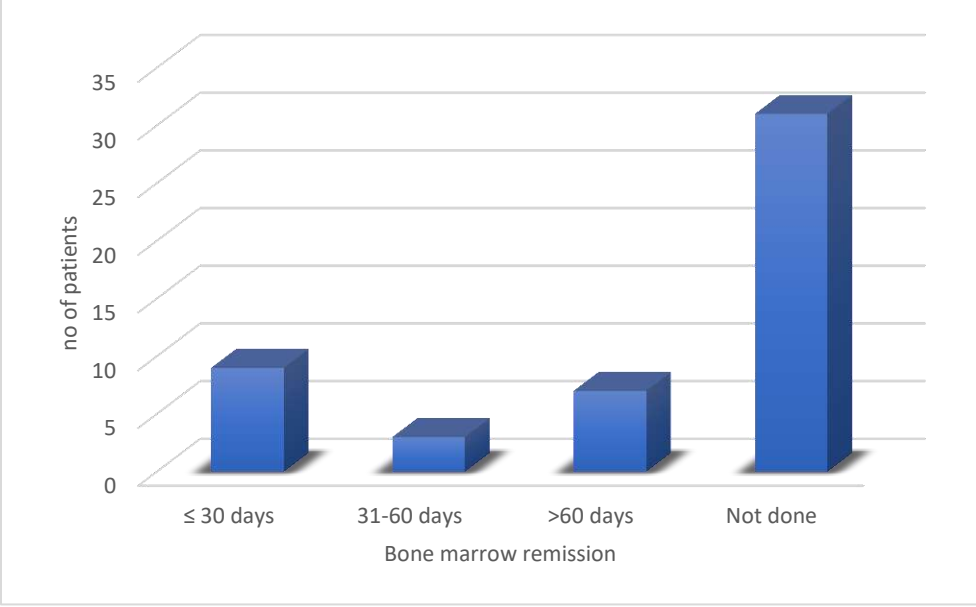


Table 17: Distribution of patients with AML with respect to outcome at first visit

	No. of patients	Percent
Discharged	32	64
DAMA	14	28
Died	4	8
Total	50	100

The table summarizes the outcomes for patients with acute myeloid leukemia (AML). Of the 50 patients, 64% were discharged after treatment, 28% left the hospital against medical advice (DAMA), and 8% died. This distribution shows that the majority of patients were successfully discharged, while a significant portion chose to leave the hospital prematurely, and a smaller percentage died.

Figure 16: Distribution of patients with AML with respect to outcome at first visit

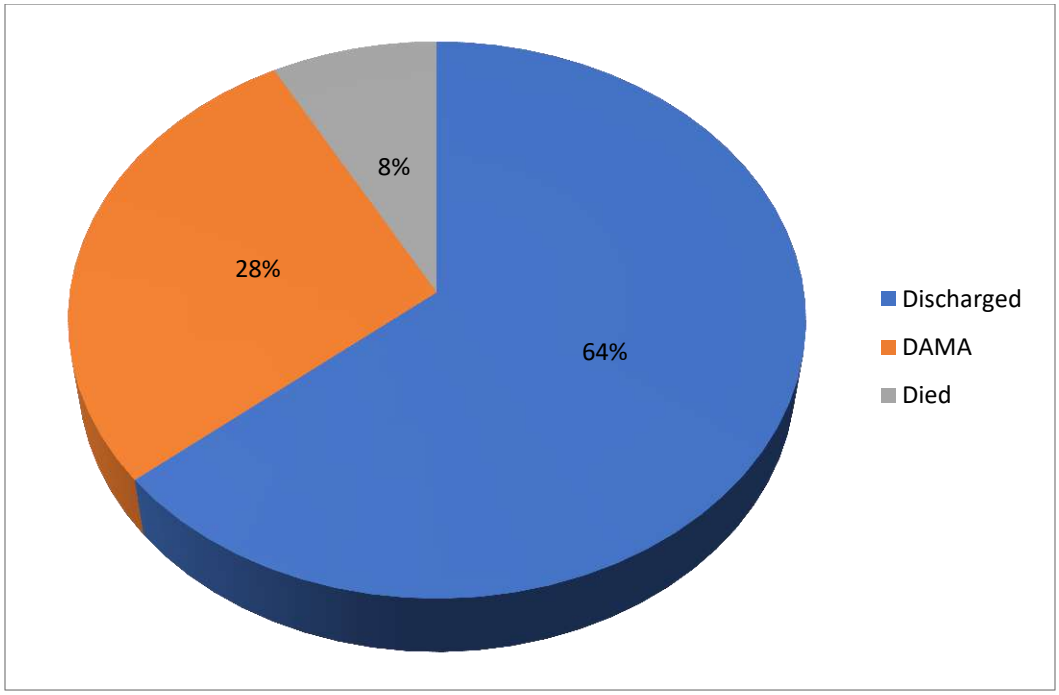


Table 18: Association of outcome at first visit with FAB subtypes

	Non M3		M3		Total		chi square	p-value
	n	%	n	%	N	%		
Discharged	25	62.5%	7	70.0%	32	64.0%	0.419	0.811
DAMA	12	30.0%	2	20.0%	14	28.0%		
Died	3	7.5%	1	10.0%	4	8.0%		
	40	100.0%	10	100.0%	50	100.0%		

62.5% of non-M3 patients were discharged, compared to 70.0% of M3 patients, with an overall discharge rate of 64.0%. 30.0% of non-M3 patients left against medical advice, compared to 20.0% of M3 patients, with an overall rate of 28.0%. 7.5% of non-M3 patients and 10.0% of M3 patients died, resulting in an overall mortality rate of 8.0%. The chi-square test for the association of outcomes with FAB subtypes shows no significant difference in outcomes between non-M3 and M3 patients (p = 0.811). This suggests that the subtype does not significantly influence the likelihood of being discharged, leaving against medical advice, or dying at first visit.

Figure 17: Association of outcome at first visit with FAB subtypes

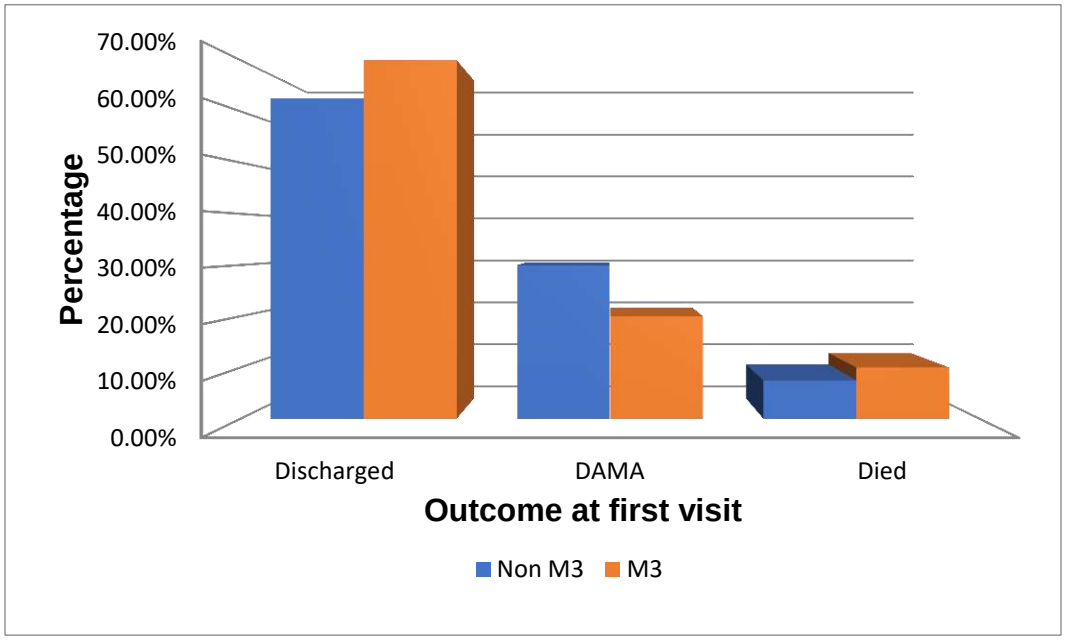


Table 19: Distribution of patients with AML with respect to follow-up after 3 months

After 3 months follow up	No. of patients	Percent
Died	16	32.0%
Lost to follow up	6	12.0%
On regular follow up	25	50.0%
Relapse	3	6.0%
Total	50	100.0%

The table shows the follow-up status of acute myeloid leukemia (AML) patients three months after treatment. Half of the patients (50%) were on regular follow-up, 32% had died, 12% were lost to follow-up, and 6% had relapsed.

Figure 18: Pie chart depicting the distribution of patients with respect to follow-up after 3 months

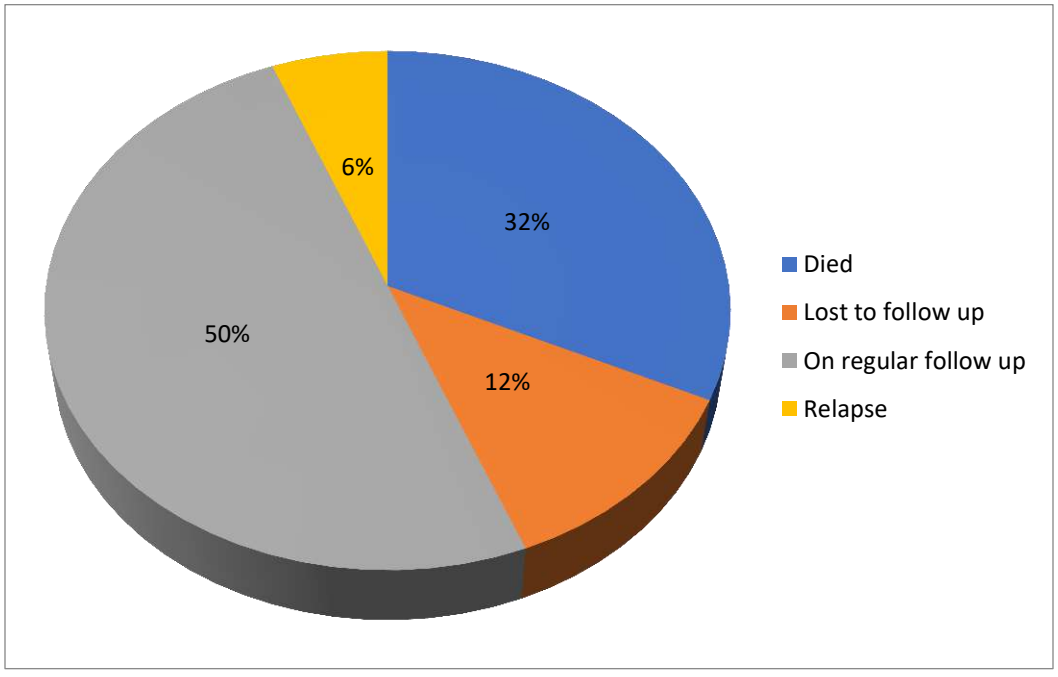


Table 20: Association of follow up outcome after three months with FAB subtypes

	non M3		M3		died		chi square	p-value
	n	%	n	%	n	%		
Died	13	32.5%	3	30.0%	16	32.0%	3.2	0.35
Lost to follow up	6	15.0%	0	0.0%	6	12.0%		
On regular follow up	18	45.0%	7	70.0%	25	50.0%		
Relapse	3	7.5%	0	0.0%	3	6.0%		
Total	40	100.0%	10	100.0%	50	100.0%		

Among the non-M3 patients, 32.5% (13 out of 40) died, while 30.0% (3 out of 10) of the M3 patients died, 15.0% of non-M3 patients (6 out of 40) were lost to follow-up, whereas none of the M3 patients were lost. For those on regular follow-up, 45.0% of non-M3 patients (18 out of 40) continued regular follow-up, compared to 70.0% of M3 patients (7 out of 10). Lastly, 7.5% of non-M3 patients (3 out of 40) experienced a relapse, with no relapses reported among the M3 patients, making the overall relapse rate 6.0%. The chi-square test and p-value suggest no statistically significant differences in outcomes between non-M3 and M3 subtypes.

Figure 19: Association of follow up outcome after three months with FAB subtypes

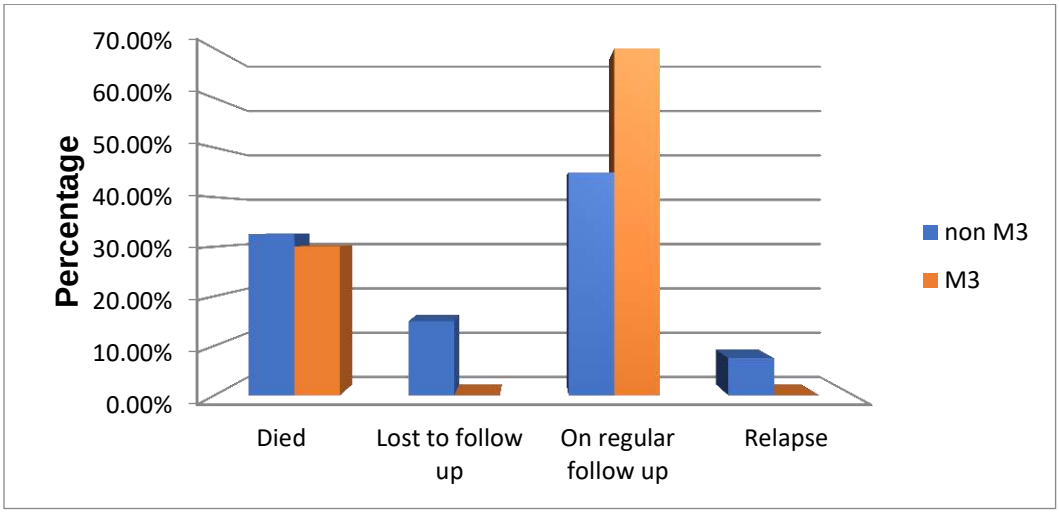


Table 21: Distribution of patients according to follow up outcome

	No. of patients	Percentage
On regular follow up	16	32.00
Died	27	54.00
Lost to follow up	7	14.00
Total	50	100

The table summarizes the followup outcome of 50 patients based on their last follow-up. It shows that 32% of the patients are on regular follow-up, indicating they are being actively monitored. However, a significant portion, 54%, have died. Additionally, 14% of the patients are lost to follow-up, meaning they have not maintained contact for further monitoring. This data highlights a high mortality rate among the patients and a need for improved follow-up mechanisms for those lost to follow-up.

Figure 20: Distribution of patients according to follow up outcome

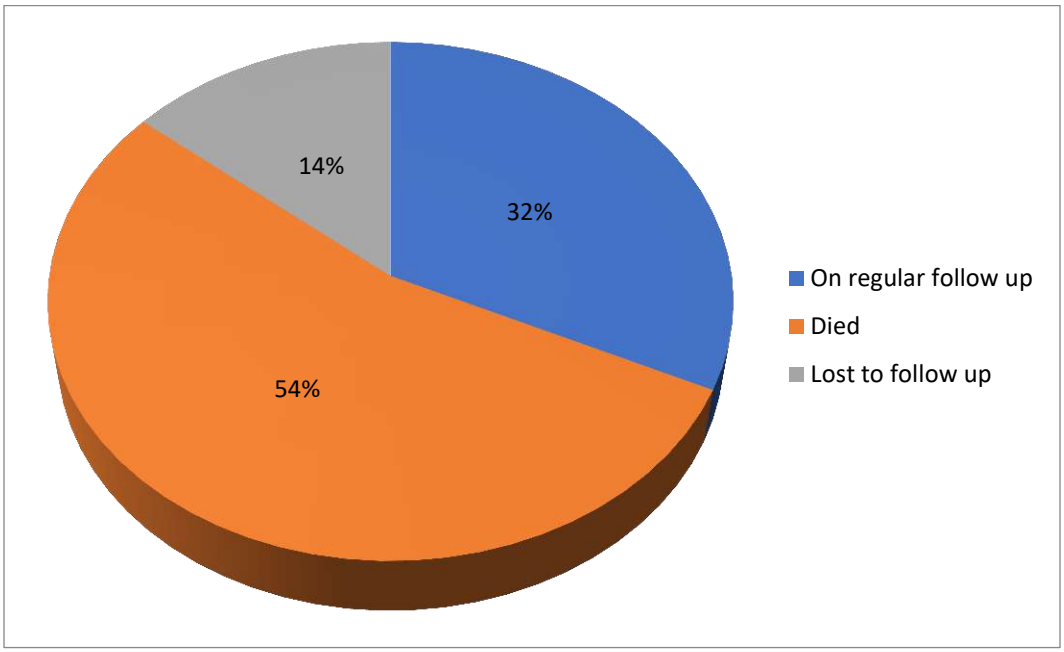


Table 22: Association of follow up outcome with FAB subtypes

	non M3		M3		died		chi-square	p-value
	N	%	n	%	n	%		
On regular follow up	10	25.0%	6	60.0%	16	32.0%	5.26	0.072
Died	23	57.5%	4	40.0%	27	54.0%		
Lost to follow up	7	17.5%	0	0.0%	7	14.0%		
Total	40	100.0%	10	100.0%	50	100.0%		

Among non-M3 patients, 25.0% (10 out of 40) were on regular follow-up, compared to 60.0% (6 out of 10) of M3 patients, resulting in an overall regular follow-up rate of 32.0%. In terms of mortality, 57.5% (23 out of 40) of non-M3 patients died, while 40.0% (4 out of 10) of M3 patients died, with an overall mortality rate of 54.0%. Additionally, 17.5% (7 out of 40) of non-M3 patients were lost to follow-up, with no M3 patients lost to follow-up, making the overall lost to follow-up rate 14.0%. The data suggests that M3 patients have a higher rate of regular follow-up and a lower rate of being lost to follow-up compared to non-M3 patients. The chi-square test indicates a trend towards significance (p = 0.072) but is not statistically significant.

Figure 21: Association of follow up outcome with FAB subtypes

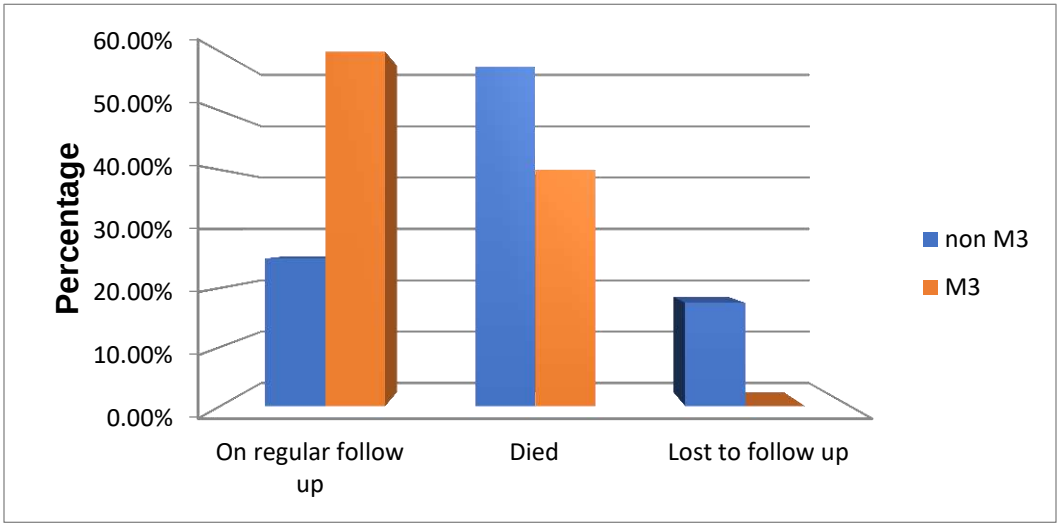


Figure 22a: Outcome of AML

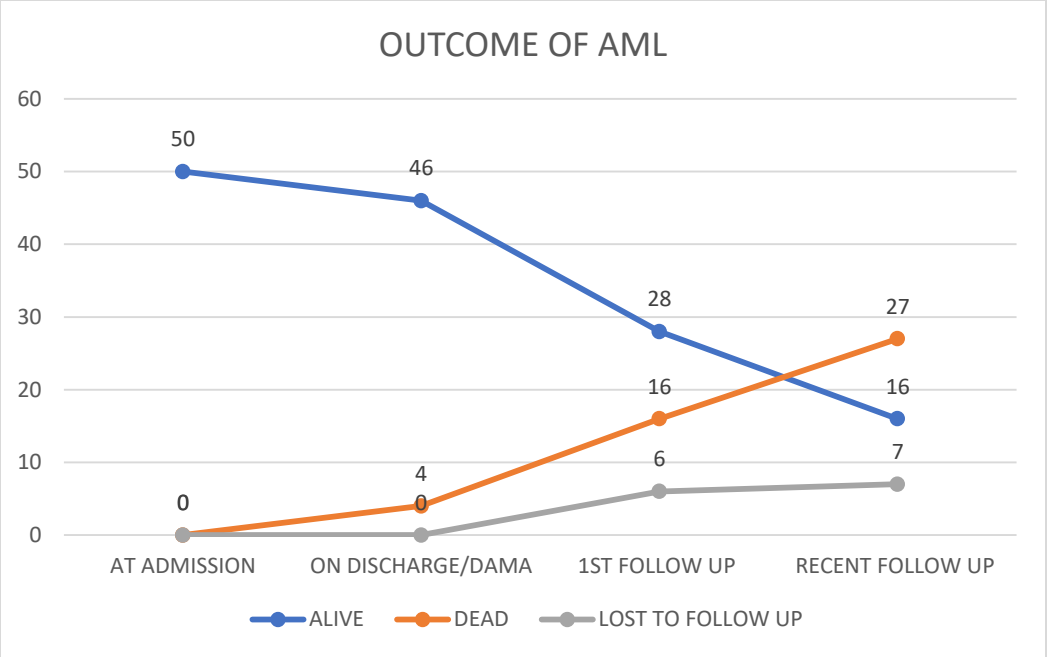
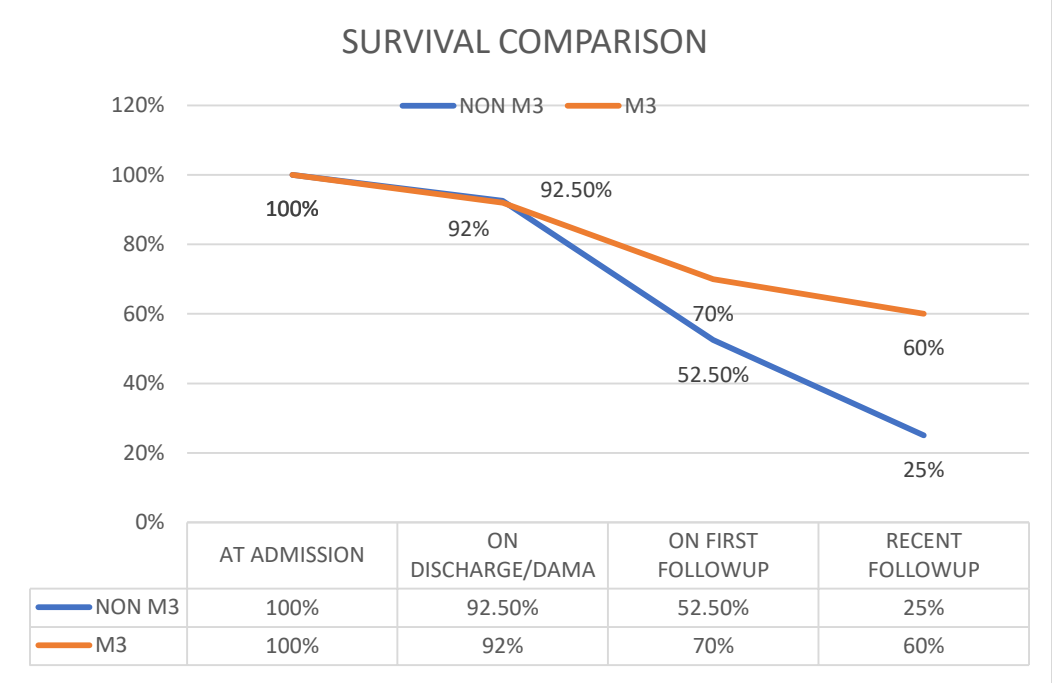


Figure 22 b: Survival comparison between M3 and non M3



	AT ADMISSION	ON DISCHARGE/DAMA	ON FIRST FOLLOWUP	RECENT FOLLOWUP
NON M3	100%	92.50%	52.50%	25%
M3	100%	92%	70%	60%

1. **Admission Overview:**
    - Total patients: 50
    - M3 subtype patients: 10 (20% of total)
    - Non-M3 subtype patients: 40 (80% of total)
2. **On Discharge/ DAMA:**
    - **Non-M3 patients:** 92.5% were discharged.
    - **M3 patients:** 92% were discharged.

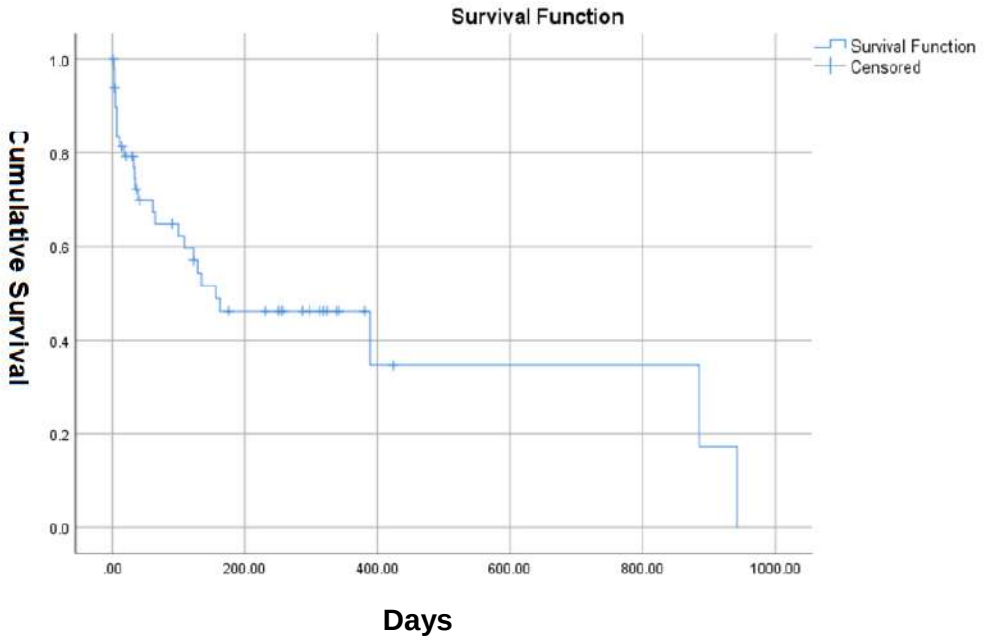
    This suggests a slightly higher discharge rate among Non M3 patients compared to M3 patients.
3. **First Follow-up (3 months):**
    - **Non-M3 patients:** 52.5% on regular follow-up.
    - **M3 patients:** 70% on regular follow-up.

    There is a notable difference, with a higher proportion of M3 patients on regular follow-up compared to Non M3 patients.
4. **Recent Follow-up:**
    - **Non-M3 patients:** 25% on regular follow-up.
    - **M3 patients:** 60% on regular follow-up.

    Again, there is a substantial difference, indicating that a larger proportion of M3 patients were on regular follow-up at the most recent assessment compared to Non M3 patients.

In summary, the study reveals that M3 subtype patients generally showed higher rates of regular follow-up at both follow-up points compared to Non M3 patients, despite similar discharge rates at the time of hospital discharge.

Figure 23: Kaplan Meier survival curve of AML Patients



The graph provided is a Kaplan-Meier survival curve, which is commonly used to estimate the survival function from lifetime data. Here's a breakdown of the graph:

Interpretation of the Kaplan-Meier Survival Curve

1. **X-Axis (Time in Days)**:
    - This axis represents the time in days.
    - The values range from 0 to 1000 days.
2. **Y-Axis (Cumulative Survival Probability)**:
    - This axis represents the cumulative survival probability, ranging from 0 to 1.
    - A value of 1 indicates 100% survival, while 0 indicates 0% survival.
3. **Survival Function**:
    - The blue step function represents the estimated survival probability over time.
    - Each step downwards represents an event (e.g., death) occurring at a particular time point.

4. **Censored Data**:
    - The small vertical ticks on the curve represent censored data points.
    - Censoring occurs when the survival time is unknown for some subjects beyond a certain point (e.g., they are lost to follow-up or still alive at the end of the study).

Observations from the Graph

- **Initial Survival**:
    - The survival probability starts at 1 (or 100%) at time zero, meaning all subjects are alive at the start of the study.
- **Steep Decline in Early Days**:
    - There is a steep decline in the survival probability initially, indicating a higher number of events (e.g., deaths) in the early period.
- **Plateaus and Declines**:
    - The survival function has several flat regions, indicating periods with no observed events.
    - There are subsequent declines at later points, showing additional events occurring over time.
- **Long-Term Survival**:
    - At around 1000 days, the survival probability approaches 0.2 (or 20%), indicating that 20% of the subjects are still surviving at this point.

Relating to the Provided Statistics

- **Mean Survival Time**:
    - The mean survival time was estimated at 393.315 days with a 95% confidence interval from 238.650 to 547.980 days.
    - The mean survival time aligns with the middle range of the survival curve, where many events have already occurred.
- **Median Survival Time**:

- The median survival time was 156 days, indicating the point at which 50% of the subjects have experienced the event.
- This is observed in the steep initial decline of the curve, suggesting that half of the subjects have an event before 156 days.

- **Censoring Impact**:
  - The numerous tick marks indicate a significant amount of censored data, impacting the estimation of survival times, especially in the later stages of the study. As a result, survival time needs a prudently interpretation. A large cohort multi centric study will help in overcoming this confounding factor.

DISCUSSION

In present prospective observational study was conducted in adults patients admitted with acute myeloid leukemia in DMCH, Ludhiana with the aim to study the clinical spectrum and short-term outcome of acute myeloid leukemia patients admitted in a tertiary care hospital.

The present study, with a mean age of 52.56±16.54 years and a median age of 55.50 years, aligns with Ordons et al.[28], who conducted a study on 45 cases with AML who were admitted in ICU at Alberta Hospital reported a mean age of 54.8 ±13.1 years in their study of 45 AML patients admitted to the ICU. However, both studies contrast with Shoukat et al.[7], who conducted a study at Jammu and Kashmir who found a significantly lower mean age of 36.69 ± 20.43 years in their study of 254 AML patients. Singh et al.[36] sourced the Data from the AML registry of the Indian Acute Leukemia Research Database (INwARD) of the Hematology Cancer from 2018-2021 and selected total of 712 patients with AML and found, the median age was 63 years. Also results from the Global Burden of Disease 2017 database showed most incidences were seen in cases aged 50 years and older which was in accordance with the present study.[37]

In contrast, Chaurasiya et al.'s[38] conducted a study at Kathmandu retrospective study on 125 adult AML patients at Kathmandu and revealed a younger patient population, with two-thirds of patients belonging to the 20-49 years age group. This finding differs significantly from the present study and others that observed a higher prevalence of AML among older adults.

Despite these variations, all studies collectively underscore the importance of considering age as a crucial factor in AML diagnosis, treatment, and prognosis. The differences in age distribution may be attributed to variations in study populations, geographic locations, and sampling methodologies.

The gender distribution of AML patients in present study shows a slight male predominance, with males constituting 52% and females 48%,

resulting in a female-to-male ratio of 1:1.08. This indicates a somewhat balanced but slightly higher prevalence of AML in males.

Comparative studies reveal a stronger male predominance in other populations. For instance, Chaurasiya et al.[38] found that 71.7% of AML cases were male, with the most affected age group being 40–49 years (24.8%) . Venkateshwaran et al.[5] observed that males constituted 58% of AML patients, with a male-to-female ratio of 1.38:1 . Similarly, Singh et al. reported a male-to-female ratio of 1.46:1 in their study of 712 AML patients

These studies suggest a consistent pattern of higher AML prevalence among males across different regions and populations, although the extent of male predominance varies.

The higher prevalence of acute myeloid leukemia (AML) in males compared to females is a multifaceted phenomenon with potential contributions from genetic, environmental, and biological factors. Environmental and lifestyle factors also contribute, with men historically having higher exposure to occupational hazards like benzene and radiation, known risk factors for AML, as documented in studies by Wong et al.[39]

In the present study, fever emerged as the most common complaint among AML patients, reported by 80% of the participants, highlighting it as a predominant symptom. Generalized weakness was the second most frequent complaint, affecting 48% of the patients. Other notable symptoms included cough, experienced by 30% of the patients, and bleeding manifestations, which were reported by 18%. Shortness of breath was a concern for 14% of the patients, while altered sensorium was the least common complaint, noted in only 2% of patients. These findings emphasize the high prevalence of fever and generalized weakness among AML patients in the study.

Comparatively, Shaukat et al.[7] found that among 174 AML patients, anemia was present in 19.5%, fever in 12.6%, and bleeding in

10.3%. Combinations of symptoms such as anemia with fever, anemia with bleeding, and fever with bleeding were observed in 12.6%, 13.2%, and 10.3% of patients, respectively. These findings suggest that individual symptoms like anemia and fever are common across different AML types. Chaurasiya et al.[38] reported that more than three-fourths of the patients exhibited pallor, while more than half had fever during admission, and lethargy/weakness was noted in over half of the cases. Recurrent infections and shortness of breath were observed in more than one-third and one-fourth of the patients, respectively.

Sultan et al.[33] conducted a study on 125 AML patients and found that the major complaints included fever in 72.8% of patients, generalized weakness in 60%, bleeding in 37.6%, and dyspnea in 12%. Similarly, Jacob et al.[34] conducted a study in a South Indian population and reported that fever was the most common symptom in 87.5% of the patients, with fatigue, bleeding manifestations, and breathlessness occurring in 20% of the patients.

The comparison reveals that fever is consistently a predominant symptom among AML patients across different studies, with the present study aligning closely with Sultan et al.[33] and Jacob et al.[34] regarding the high prevalence of fever. Generalized weakness also shows a high prevalence, consistent with Sultan et al.[33] and Chaurasiya et al.[38], though Jacob et al.[34] reported a lower prevalence of fatigue. Bleeding manifestations vary more widely in prevalence across studies, but the present study's findings are in line with those of Sultan et al.[33] and Jacob et al.[34] Shortness of breath shows similar prevalence to Sultan et al.[33] but is lower than reported by Chaurasiya et al.[38] The presence of altered sensorium, reported in only 2% of patients in the present study, was not prominently noted in other studies. These comparisons underscore the variability in symptom prevalence among AML patients across different populations and study methodologies.

In the present study, it was found that the majority (82%) of AML cases did not experience any bleeding. Among the 18% who did report bleeding, various types were observed, each affecting a small portion of the sample: gum bleeding and intracerebral hemorrhage were reported by 4% of patients each, while lower gastrointestinal bleeding, malena, menorrhagia, subdural hematoma, and nasal bleeding were each reported by 2% of patients. This indicates that while bleeding was relatively uncommon, those who did experience it faced diverse and serious types.

Comparatively, Chaurasiya et al.[38] found that nearly one-fourth of their cases had bruising (24.8%) and abnormal mucosal bleeding (23.4%). Jacob et al. reported bleeding manifestations in 20% of their AML patients. The comparison shows that the present study has a lower overall prevalence of bleeding (18%) compared to the findings of Chaurasiya et al.[38] (24.8% for bruising and 23.4% for mucosal bleeding) and is slightly lower than Jacob et al. (20%). The types of bleeding reported in the present study are more varied, while Chaurasiya et al.[38] focused on specific types like bruising and mucosal bleeding.

In the present study, pallor was a common finding in 52% of the patients, while icterus was rare, seen in only 4%. Systemic examination showed that In central nervous system (CNS) status, 96% of patients had normal findings, with 2% showing a decreased Glasgow Coma Scale (GCS). Abdominal examination revealed that 78% of patients had normal findings, whereas 22% had hepatomegaly and splenomegaly. Additionally, respiratory examination auscultation findings (crepts, bronchial breathing or wheeze) were noted in 54% of the patients.

Chaurasiya et al.[38] observed hepatosplenomegaly in 17.9% of patients, and 16.6% of AML patients complained of bone pain.

Overall, the present study and other comparative studies highlight pallor as a frequent finding among AML patients. However, the prevalence rates vary, with Jacob et al.[34] reporting the highest rate of pallor (95%). Additionally, hepatosplenomegaly is commonly reported across studies,

though the rates differ, with the present study showing a higher prevalence (22%) compared to Chaurasiya et al.[38] (17.9%).

Comparing the findings from the present study with those reported by Jacob et al.[34], Sultan et al.[33], and Shaukat et al.[7] reveals both similarities and notable differences across various hematologic and biochemical parameters in patients with acute myeloid leukemia (AML). In terms of total leukocyte count (TLC), the present study shows a mean ± SD of 34.40 ± 40.79 × 10^9/L and a median of 22.45, which aligns broadly with the median reported by Jacob et al. (38.9 × 10^9/L) and the mean reported by Sultan et al.[33] (43.08 ± 68.45 × 10^9/L), indicating variability but generally comparable ranges.

Hemoglobin levels (HB) in the present study average 7.14 ± 1.87 g/dL with a median of 7.00 g/dL, which shows moderate variability similar to Sultan et al.[33] (8.19 ± 2.12 g/dL) but notably higher than the mean reported by Shaukat et al.[7] (5.84 g/dL). Platelet counts in the present study average 69.63 ± 96.66 × 10^9/L with a median of 40.00 × 10^9/L, indicating considerable variability compared to Jacob et al.[34] (median of 38.9 × 10^9/L) and Sultan et al.[33] (62.32 ± 78.61 × 10^9/L). Other biochemical parameters such as PTI, INR, bilirubin levels, liver enzymes, and electrolytes show varying degrees of consistency and divergence across the studies, reflecting the heterogeneity in patient populations, study methodologies, and possibly regional or demographic factors influencing these parameters.

In present study HRCT was not done for 40% of patients. Among those who had HRCT, the most common finding was Superadded Infection (probable bacterial/viral infection) (34%). Other findings included fungal infection (10%), no abnormalities (10%), pleural/pericardial effusion (4%), and fluid overload alone (2%). This indicates a variety of complications detected through HRCT in AML patients undergoing treatment.

Comparing the findings from Bugdaci et al. with the present study on pulmonary radiological findings in AML patients reveals several notable differences and some similarities in the types and prevalence of detected complications. Bugdaci et al. reported that 19% of AML patients experienced respiratory events, primarily due to infections, alongside complications like leukemic infiltration, pulmonary embolism, and pneumothorax. In contrast, the present study found that among patients who underwent HRCT, Superadded Infection (probable bacterial/viral infection) were the most common findings (34%), followed by fungal infections (10%) and pleural/pericardial effusions (4%). This indicates a higher prevalence of infectious complications detected through HRCT in the present study compared to Bugdaci et al.'s findings. Overall, while Bugdaci et al. focused on specific complications and radiographic patterns, the present study provides a comprehensive view of diverse HRCT findings in AML patients, underscoring the multifaceted nature of pulmonary complications in this population.

In present study among those who underwent the test, 4% had systolic dysfunction, while 78% had a normal Left Ventricular Ejection Fraction (LVEF) of 60%, indicating normal heart function.

Several factors may explain the prechemotherapy myocardial remodeling in AML patients. It had been confirmed that the imbalance between pro-inflammatory and anti-inflammatory cytokines is an important reason for the formation of leukemia blasts. Elevated plasma CRP levels were found in most AL patients [41]. The activation of inflammation in the heart causes LV remodeling and dysfunction and is associated with adverse outcomes in patients with heart failure. Another possible mechanism to explain cardiac alterations in patients with AL is direct infiltration of the heart by leukemic cells, which has been extensively described in previous autopsy studies [42-43].

Zhang et al.[44], in 2023) found that even newly diagnosed AML patients without prior chemotherapy can exhibit decreased left ventricular

global longitudinal strain (LVGLS), a marker of systolic dysfunction. However, many of these patients still had normal LVEF.

In the present study, the most commonly expressed markers in AML patients were CD13 (70%), CD117 (68%), and CD33 (60%). HLADR and CD38 were each present in 54% of the patients, CD34 in 40%, and CD123 in 36%. MPO (myeloperoxidase) was noted in 32%, and CD64 in 20%. Less common markers included CD14 (8%) and CD11b found in 6%. The least expressed marker was CD10, at 4%.

Venkateshwar et al.[5] studied the immunophenotype of 38 cases of AML and found that CD33, CD13, CD117, and CD64 were the most commonly expressed myeloid antigens. Early myeloblasts expressed CD34 and HLA-DR, but these markers were lost by the promyelocyte stage. In their study, 52.63% of cases were positive for CD34, which is higher than the 40% positivity observed in the present study for CD34 but consistent with the general trend of high expression of CD33, CD13, and CD117.

Shaukat et al.[7] flow cytometry analysis revealed the following positive marker percentages:

The study by Shaukat et al.[7] reported the following positive marker percentages in AML patients: CD11b was positive in 25.3% of samples, CD11c in 9.7%, and CD13 showed a high positivity rate of 87.9%. CD15 was positive in 50.0% of samples, while CD19 had a positivity rate of 12.8%. CD33 exhibited the highest positivity at 95.0%, followed by CD34 at 54.6% and CD36a at 18.6%. CD41 had a low positivity rate of 3.2%, whereas CD45 was positive in 88.9% of samples. CD56 was positive in 11.6% of samples, CD61 in 2.1%, CD64 in 48.8%, and CD113 in 4.7%. CD117 showed a high positivity rate of 83.8%, CD123 in 46.0%, and MPO (myeloperoxidase) had a positivity rate of 89.0%.

Compared to Shaukat et al.[7], the present study shows lower percentages for several markers. CD13, CD33, and CD117 had high positivity rates in both studies, but Shaukat et al. reported higher rates

(87.9% for CD13, 95.0% for CD33, and 83.8% for CD117) compared to 70%, 60%, and 68%, respectively, in the present study. CD34 was also more commonly expressed in Shaukat et al.[7] study (54.6%) compared to 40% in the present study. Similarly, MPO had a much higher positivity in Shaukat et al.[7] study (89.0%) compared to 32% in the present study.

Hanson et al.[45], Terstappen LWM et al.[46], Roberts et al.[47], San Miguel et al.[48], Kaleem et al.[49], and Auewarakul et al.[50] also demonstrated that CD33, CD13, CD117, and CD64 were the most commonly expressed myeloid antigens in their studies of AML. This aligns with the findings of the present study and Venkateshwar et al.[5], but the percentage of positive cases can vary.

- **HLA-DR and CD38**: Present in 54% of patients in the current study, consistent with the expression of early myeloid markers. Other studies may not provide a direct comparison for these markers.
- **CD64**: Present in 20% of patients in the current study, significantly lower than the 48.8% observed in Shaukat et al.'s study.
- **CD123**: Present in 36% of patients in the current study, compared to 46% in Shaukat et al.'s study.
- **CD34**: Found in 40% of the current study's patients, while Shaukat et al. reported a higher positivity of 54.6%.
- **CD11b and CD10**: Both low in the current study (6% and 4% respectively) compared to Shaukat et al.'s results where CD11b was 4.7%, indicating some consistency for rare markers.

The present study and previous research consistently highlight CD33, CD13, and CD117 as commonly expressed markers in AML patients. However, the exact percentages vary, likely due to differences in sample sizes, patient populations, and methodologies. Shaukat et al. reported generally higher positivity rates for most markers compared to the present study. CD34, HLA-DR, and CD64 show notable variation in

expression between studies, reflecting the heterogeneity of AML and the influence of disease stage and patient characteristics.

The present study found the most common subtypes to be M2 (28%) and M4 (24%), followed by M3 (20%). Less frequent subtypes included M0/M1 (16%), M1 (8%) and M5 (4%). This indicates a higher prevalence of M2 and M4 among the patients, with M3 also being significant. Specifically, 20% were diagnosed with M3 AML, while 80% were diagnosed with non-M3 AML, highlighting a considerable presence of the M3 subtype.

In comparison, Venkateshwar et al.[5] reported the distribution of AML subtypes as M0: 2 cases (6.9%), M1: 17 cases (58.6%), M2: 6 cases (20.7%), and M3: 4 cases (13.8%). Here, M1 was the most common subtype, followed by M2, M3, and M0, differing from the present study, which found M2 and M4 to be the most prevalent.

Sultan et al.[33] identified AML-M1 as the most common type, followed by M2, M3, M4, and M0. This aligns somewhat with the present study's findings regarding the frequency of M1 and M2 but shows a shift from M2 to M1 as the dominant subtype in their cohort. Their findings suggest a transition from the M2 subtype to the M1 variant, which is consistent with recent studies in Pakistan that also found M1 to be predominant (Hamayun et al., 2005)[51].

Shaukat et al.[7] showed that around one-fourth of patients were APML (25%), treated with the standard ICAPL-2006 protocol, and 75% were non-M3. This aligns with the present study's findings regarding the significant presence of M3 but contrasts with the overall distribution of subtypes.

In the present study, markers like HLADR show significant differences in expression between non M3 (26.00%) and M3 (10.0%) groups, with a chi-square value of 9.74 and a p-value of 0.00, suggesting a statistically significant association between HLADR expression and group membership. Similarly MPO and CD 64 shows significant

differences in expression between non M3 and m3 groups. Conversely, markers like CD117 show less variability between groups (67.00% in non M3 vs. 70.00% in M3) with a non-significant chi-square value (0.02) and high p-value (0.88), indicating no significant association with group. Overall, this table provides insights into how CD marker expression profiles differ between the non M3 and M3 groups and the statistical significance of these differences.

Markers such as CD13, CD34, and CD38 showed no significant association with either AML subtype, indicating similar expression patterns across non-M3 and M3 cases. The data highlight specific markers, particularly HLADR, MPO, and CD64, which could serve as potential diagnostic indicators differentiating between non-M3 and M3 AML.

In a study by Venkateshwaran et al.[5], 1 out of 4 cases of AML-M5(non M3) in our study expressed CD14, and none of the AML-M4(non M3) cases showed CD14 expression. This antigen expression is not restricted to acute leukemia with monocytic differentiation. Acute Promyelocytic leukemia (AML-M3) is an unusual and distinctive disease clinically, morphologically, immunophenotypically, and even genotypically. As previously reported, the majority of cases of AML express HLA-DR. The clear exception to this rule is AML-M3, in which only rare cases are reported to be positive. In this study, 1 out of 10 cases of AML-M3 expressed HLA-DR, whereas 3 cases showed CD34 expression. None of our AML-M3 cases showed CD2 expression, though positivity for this T cell marker has been well documented in AML-M3, and the presence of this antigen has even been associated with specific breakpoints within the t(15;17) translocation.

In present study RT-PCR panel was performed in 23(32%) patients with AML. While it was negative for 7 cases. And wasn't performed for 27 cases. About the distribution and prevalence of specific genetic mutations identified through RT-PCR in the study cohort, we found that NPM-1 is the most frequently detected marker, found in 34% of AML patients, with 34 %

cases in non M3 and no case in M3 patients. FLT3 Detected in 8.6% of AML patients, with 8.6% cases in Non M3 and no case in M3 patients. PML-RARA Detected in 17% of AML patients, with 17% cases in M3 and no case in Non M3 patients. FLT3-D835 Found in 8.6 % of AML patients, with 4.3% cases in M3 patients and 4.3% cases in Non M3 patients. FLT3-ITD Detected in 13% of AML patients, with 4.3% cases in Non M3 and 8.6% cases in M3. CBFB-MYH11 Detected in 13% of AML patients, with 13% cases in Non M3 and no case in M3 patients. Certain genetic markers, such as NPM-1, FLT3, and CBFB-MYH11, are present in non-M3 patients but absent in M3 patients. Conversely, PML-RARA and FLT3-ITD is more prevalent in M3 patients compared to non-M3 patients. These findings suggest distinct genetic profiles between the two subtypes, with some markers being subtype-specific.

The present study and the referenced studies by Koczkodaj et al.[52], Backer et al.[53], and Thiede et al.[54] provide comprehensive insights into the genetic mutations prevalent in acute myeloid leukemia (AML). In the present study, RT-PCR analysis was performed on 32% of AML patients, revealing NPM-1 as the most frequently detected mutation (16%), whereas FLT3 and FLT3-D835 were the least common (4%). The Non M3 group showed a diverse range of mutations, with 100% prevalence for NPM-1 and FLT3 mutations and no PML-RARA mutations. Conversely, the M3 group had no NPM-1 or FLT3 mutations but exhibited a 100% prevalence for the PML-RARA mutation.

Koczkodaj et al.[52] reported chromosomal abnormalities in 64% of their AML patients, with FLT3-ITD and NPM-1 mutations detected in 8% and 6% of patients, respectively. They emphasized the association of NPM-1 mutations with a normal karyotype (CN-AML) and longer relapse-free survival. Backer et al.[53] found that NPM-1 mutations significantly improve prognosis, particularly in older patients without concomitant FLT3-ITD mutations. Thiede et al.[54] highlighted the frequent coexistence of

NPM-1 and FLT3-ITD mutations, noting that NPM-1 mutations typically precede FLT3-ITD mutations.

A study by sultan et al.[33] reported Clinically, an AML patient with an increase percentage of leukemic blasts tends to have FLT3-ITD mutation (Gregory et al. [55], 2009). Recently Mawali et al showed that half of the patients with M1-FAB subtype had FLT3/ITD positivity which has been associated with poor prognosis (Mawali et al.[56], 2013).

While the present study emphasizes the distinct genetic profiles between Non M3 and M3 AML groups, the referenced studies corroborate the significant prognostic value of NPM-1 mutations and their common coexistence with FLT3-ITD mutations, contributing to a better understanding of the molecular landscape and prognosis in AML.

Acute promyelocytic leukemia (APL) is a distinct subtype of acute myeloid leukemia (AML) characterized by its unique molecular pathogenesis, clinical manifestations, and treatment protocols. This type of leukemia is defined cytogenetically by a balanced translocation between chromosomes 15 and 17, denoted as t(15;17)(q24;q21) . This translocation involves the retinoic acid receptor alpha (RARA) gene on chromosome 17 and the promyelocytic leukemia (PML) gene on chromosome 15, resulting in the creation of a PML-RARA fusion gene.[57-58]

The PML-RARA fusion gene plays a crucial role in the pathogenesis of APL by disrupting normal cellular processes, leading to the accumulation of immature promyelocytes. This fusion gene interferes with the normal function of RARA, a nuclear receptor that regulates gene expression involved in cellular differentiation and proliferation. As a result, the cellular transformation occurs, which is a hallmark of APL.[57-58]

One of the notable aspects of APL is its sensitivity to treatment with differentiating agents. The introduction of all-trans-retinoic acid (ATRA) combined with chemotherapy or arsenic trioxide (ATO) has significantly improved the prognosis for APL patients. These treatments target the

PML-RARA fusion protein, promoting the differentiation and maturation of the leukemic cells into non-proliferative cells. Consequently, APL, once considered a fatal disease, now boasts cure rates of approximately 90% for both pediatric and adult patients.[57]

In the present study, a majority of patients (54%) were treated with hypomethylating agents (HMAs), either alone or in combination with Venetoclax. A significant proportion (18%) did not undergo any treatment. The remaining patients were treated with arsenic trioxide (ATO), all-trans-retinoic acid (ATRA), mitoxantrone, idarubicin, or the daunorubicin plus cytarabine (7+3) regimen.

In a study by Chaurasiya et al.[38], more than half of the cases (62.8%) were treated with chemotherapy alone, while 2.1% underwent bone marrow transplants. The study also highlights the emerging role of targeted therapies such as Venetoclax, a BCL-2 inhibitor, which can be used alone or in combination with other chemotherapeutic agents. Additionally, the potential role of CAR-T cells in the treatment of AML was noted.

In a study by Singh et al.[36], the first-line therapy consisted of HMAs in 239 (73.9%) patients and the 7+3 induction regimen or its modifications in 60 (18%) patients. Within the HMA group, Azacytidine was used in 184 (76.9%) patients and Decitabine in 55 (23.01%) patients. A minority (7.4%) received alternate intensive or low-dose regimens. Additionally, 79 patients (24%) received targeted oral agents as part of either first-line or subsequent therapy, with most receiving these agents in combination with HMAs. Venetoclax was the most commonly used targeted agent (n = 66).

In the current study, the majority of patients (54%) were treated with hypomethylating agents, either alone or in combination with Venetoclax. This contrasts with findings from Chaurasiya et al.[38], where a significant proportion (62.8%) received chemotherapy alone, reflecting a preference for traditional chemotherapy regimens without the addition of targeted

therapies like Venetoclax. Conversely, Singh et al.[36] reported a higher uptake of hypomethylating agents (73.9%) as first-line therapy, with a substantial portion (24%) also receiving targeted oral agents such as Venetoclax, often in combination with HMAs.

Among the 50 patients studied, 38 % achieved bone marrow remission. Of these, 18 % achieved remission within 30 days, 6 % within 31-60 days and 14% took more than 60 days. However, 62 % of the patients were not assessed for bone marrow remission. Of the 50 patients, 64 % were discharged after treatment , 28% left the hospital against medical advice (DAMA) and 8 % died. This distribution shows that the majority of patients were successfully discharged, while a significant portion chose to leave the hospital prematurely and a smaller percentage died.

Also we found that AML subtype does not significantly influence the likelihood of being discharged, leaving against medical advice, or dying after the first visit.

After 3 months of follow up, half of the patients (50%) were on regular follow-up, 32% had died, 12% were lost to follow-up, and 6% had relapsed. Among the non-M3 patients, 32.5% (13 out of 40) died, while 30.0% (3 out of 10) of the M3 patients died, resulting in an overall mortality rate of 32.0%. 15.0% of non-M3 patients (6 out of 40) were lost to follow-up, whereas none of the M3 patients were lost, making the overall rate of lost to follow-up 12.0%. For those on regular follow-up, 45.0% of non-M3 patients (18 out of 40) continued regular follow-up, compared to 70.0% of M3 patients (7 out of 10), resulting in an overall regular follow-up rate of 50.0%. Lastly, 7.5% of non-M3 patients (3 out of 40) experienced a relapse, with no relapses reported among the M3 patients, making the overall relapse rate 6.0%. as per recent follow up it was found that It shows that 32% of the patients are on regular follow-up, indicating they are being actively monitored. However, a significant portion, 54%, have died. Additionally, 14% of the patients are lost to follow-up, meaning they

have not maintained contact for further monitoring. Also, we found that Among non-M3 patients, 25.0% (10 out of 40) were on regular follow-up, compared to 60.0% (6 out of 10) of M3 patients, resulting in an overall regular follow-up rate of 32.0%. In terms of mortality, 57.5% (23 out of 40) of non-M3 patients died, while 40.0% (4 out of 10) of M3 patients died, with an overall mortality rate of 54.0%. Additionally, 17.5% (7 out of 40) of non-M3 patients were lost to follow-up, with no M3 patients lost to follow-up, making the overall lost to follow-up rate 14.0%. The data suggests that M3 patients have a higher rate of regular follow-up and a lower rate of being lost to follow-up compared to non-M3 patients.

Jacob et al.[34] reported a relapse rate of 46% over a median follow-up period of 9 months in their study. This rate is comparable to a 44% relapse rate reported by Tata Memorial Hospital, Mumbai, although their follow-up period was significantly longer at 36 months[26]. The higher relapse rates observed in these studies could be attributed to factors such as uniform consolidation therapy for patients with varying risk profiles and limited access to allogeneic transplantation. The comparison across various registries and studies sheds light on the evolving landscape of acute myeloid leukemia (AML) treatment outcomes and patient demographics.

In the present study, the mortality rates highlight significant challenges in managing AML, with 57.5% of non-M3 patients and 40.0% of M3 patients succumbing to the disease, resulting in an overall mortality rate of 54.0%. Jacob's study[34] underscores even higher mortality rates, with 70% mortality across all FAB subtypes, including an alarming 85% mortality specifically in AML M3 cases. The distribution of deaths throughout treatment phases—before induction, during induction, consolidation, and due to relapse—further illustrates the critical stages where interventions are crucial.

Comparatively, the Swedish AML Registry (2009) reported a median survival of 196 days among patients aged 72 years, with a

substantial 62% undergoing induction chemotherapy (IC) and an early mortality rate of 19% within 30 days. In contrast, the SEER Database (2013)[59] highlighted a relative survival of 20% in older patients, while the Danish Registry (2020)[60] revealed varying early mortality rates (16% to 54% within 60 days) across different age groups, emphasizing the impact of age on treatment outcomes. European registries (2022) continued to document challenges, with a 19.4% early mortality rate within 60 days despite advancements in treatment protocols.

The HCC-InWARD Registry (2022)[36] further underscores disparities in treatment approaches, with 31% early mortality within 60 days despite a lower 18% IC rate. These findings collectively underscore the complex interplay of patient demographics, treatment protocols, and survival outcomes across different cohorts and timeframes. The data highlights ongoing efforts to enhance survival rates and reduce early mortality in AML, particularly in older populations where the disease presents significant clinical challenges.

SUMMARY AND CONCLUSION

The study conducted at DMCH, Ludhiana, provided insights into the clinical spectrum and short-term outcomes of acute myeloid leukemia (AML) patients in a tertiary care hospital setting.

- Majority of AML patients are older, with 40% over 60 years and 20% in the 51-60 age group; median age is 54 years (IQR: 37-66).
- 52% of patients are male, and 48% are female.
- Most common complaints are fever (80%) and generalized weakness (48%).
- 18% of patients reported various types of bleeding, with gum bleeding and intracerebral hemorrhage being most common (4% each).
- Pallor present in 52% of patients, normal heart sounds in all, and hepatomegaly and splenomegaly in 22%.
- Median TLC is 22.45, hemoglobin is 7.00, and platelet count is 40.00.
- 40% of patients did not undergo HRCT; 34% had bacterial/viral infections.
- 78% had normal LVEF of 60%, and 4% had systolic dysfunction.
- Most common markers were CD13 (70%), CD117 (68%), and CD33 (60%).
- Most common subtypes are M2 (28%) and M4 (24%).
- NPM-1 is the most frequently detected marker (16%).
- Majority treated with hypomethylating agents (54%); 18% did not undergo treatment.
- Among the 50 patients, 20% were diagnosed with M3 AML, while 80% were diagnosed with non-M3 AML.
- Flow cytometry analysis showed significant associations with HLADR, MPO, and CD64 markers, indicating potential diagnostic indicators for differentiating between M3 and non-M3 AML.

- RT-PCR panel results highlighted that NPM-1 was the most frequently detected marker, especially in non-M3 patients, while PML-RARA was specific to M3 patients.
- In terms of treatment, 54% of patients were treated with hypomethylating agents, either alone or with Venetoclax.
- Bone marrow remission was achieved by 38% of patients, with varying time periods required. Outcomes indicated that 64% of patients were discharged, 28% left against medical advice, and 8% died.
- Follow-up after three months revealed that 50% of patients were on regular follow-up, 32% had died, 12% were lost to follow-up, and 6% had relapsed
- . The study also showed that non-M3 patients had a higher mortality rate (57.5%) compared to M3 patients (40%), and a higher rate of being lost to follow-up. However, M3 patients had a higher rate of regular follow-up (60%) compared to non-M3 patients (25%).
- The mean survival time was estimated at 393.315 days with a 95% confidence interval from 238.650 to 547.980 days. The mean survival time aligns with the middle range of the survival curve, where many events have already occurred. The median survival time was 156 days, indicating the point at which 50% of the subjects have experienced the event. This is observed in the steep initial decline of the curve, suggesting that half of the subjects have an event before 156 days.

- Overall, the findings suggest distinct clinical profiles and outcomes for M3 and non-M3 AML patients, with specific genetic markers and treatment responses highlighting the need for tailored therapeutic approaches.

The present study is crucial as it provides a comprehensive understanding of AML patient demographics, clinical presentations, and outcomes in an Indian tertiary care context, which is often underrepresented in global research. The findings underscore the significant challenges in managing AML, particularly the high early mortality rates and the variability in treatment responses based on genetic profiles. By identifying specific genetic markers and their associations with AML subtypes, the study offers valuable information that can guide personalized treatment strategies, ultimately aiming to improve patient outcomes. Furthermore, the study highlights the need for enhanced diagnostic tools, better follow-up care, and access to advanced treatment options like allogeneic transplantation, advocating for systemic improvements in AML management and patient care infrastructure.

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							CHIEF COMPLAINTS						GENERAL EXAMINATION							
S.No.	MRD NO	Intials	AGE (Years)	SEX	DATE OF ADMISSION	DATE OF DIAGNOSIS	FEVER	COUGH	SHORTNESS OF BREATH	ALTERED SENSORIUM	GENERALISED WEAKNESS	BLEEDING MANIFESTATION	PALLOR	ICTERUS	Spo2 (%)	HEART RATE(BPM)	RESP RATE (PER MIN)	SBP(mmhg)	DBP(mmhg)	BODY TEMP(f)
1	1452904	CL	67	MALE	1/28/2023	1/28/2023	YES	NO	NO	NO	NO	-	NO	NO	94	94	30	118	70	98.4
2	1461789	UJ	71	FEMALE	2/12/2023	1/13/2023	YES	NO	YES	NO	NO	-	YES	NO	98	112	32	112	70	100
3	1433542	HK	22	FEMALE	12/20/2022	12/23/2022	NO	NO	NO	NO	YES	-	YES	NO	94	114	26	100	70	98.6
4	1440881	MS	28	FEMALE	1/2/2023	1/3/2023	NO	YES	NO	NO	YES	-	YES	NO	98	116	24	100	60	99.6
5	1427309	MS	33	MALE	12/6/2022	12/7/2022	YES	YES	YES	NO	NO	-	NO	NO	96	110	28	99	110	69
6	1436038	AS	18	MALE	12/22/2022	12/23/2023	NO	NO	NO	NO	YES	-	NO	NO	98	90	18	118	74	98.9
7	1469309	VS	52	MALE	2/24/2023	2/28/2023	YES	YES	NO	NO	YES	-	YES	NO	99	136	26	100	70	101
8	1431820	KLS	49	MALE	12/16/2023	12/15/2022	YES	NO	NO	NO	YES	-	YES	NO	94	110	28	136	78	99.8
9	1452305	JS	25	MALE	1/27/2023	1/28/2023	YES	NO	NO	NO	YES	-	YES	NO	99	86	16	126	82	98.2
10	1480877	SB	32	FEMALE	3/14/2023	3/17/2023	YES	YES	NO	YES	NO	YES(ICH)	YES	NO	99	68	26	170	96	99
11	1462145	GS	47	MALE	2/13/2023	2/14/2023	YES	NO	NO	NO	YES	-	YES	NO	98	74	28	110	78	98
12	1486200	SV	55	FEMALE	3/23/2023	3/25/2023	YES	NO	NO	NO	YES	-	NO	NO	98	84	20	116	76	97.6
13	1471380	KK	65	FEMALE	2/27/2023	3/2/2023	YES	NO	NO	NO	NO	-	NO	NO	96	84	16	138	80	99
14	1487384	NR	51	FEMALE	3/25/2023	4/5/2023	YES	NO	NO	NO	NO	-	YES	NO	99	110	22	110	70	99
15	1498895	BS	72	MALE	4/13/2023	4/15/2023	NO	YES	NO	NO	YES	-	NO	NO	99	112	28	120	80	98.4
16	1505569	NB	53	MALE	4/25/2023	4/27/2023	YES	NO	YES	NO	NO	-	NO	NO	96	118	28	130	90	100
17	1511450	KK	59	FEMALE	4/17/2023	4/18/2023	NO	NO	NO	NO	YES	-	YES	NO	99	76	20	110	70	98
18	1498893	RS	34	MALE	4/13/2023	4/17/2023	YES	NO	NO	NO	YES	-	YES	YES	96	126	26	130	70	100
19	1507011	SP	66	MALE	4/27/2023	5/9/2023	YES	NO	NO	NO	YES	-	NO	NO	99	88	16	126	74	96
20	1523474	GS	66	MALE	5/20/2023	5/26/2023	NO	NO	NO	NO	YES	-	NO	NO	96	84	12	126	74	98
21	1489323	M	24	FEMALE	3/28/2023	30-Mar	YES	YES	NO	NO	YES	YES (MENORRHAGIA)	NO	NO	99	78	22	90	60	98

			SYSTEMIC EXAMINATION																		
S.No.	MRD NO	Intials	RESPIRATORY	ABDOMEN	CVS	CNS	TLC	HB	PLATELET	PTI	INR	BIL (t)	BIL(d)	SGOT	SGPT	ALP	CREATININE	Na	K	Cl	Calcium
1	1452904	CL	B/L COARSE CREPTS	SOFT, HEPATOMEGALY AND SPLENOMEGALY	S1 S2 HEARD	NORMAL	97.3	7.6	14	17	1.3	0.32	0.17	21	15	60	2.32	134	3.53	104	7.9
2	1461789	UJ	B/L DECREASED AIR BASAL AREAS	SOFT, HEPATOMEGALY AND SPLENOMEGALY	S1 S2 HEARD	NORMAL	151.1	5.4	150	17.6	1.61	0.96	0.43	46	37		9.3	145	3.4	107	8.5
3	1433542	HK	AIR ENTRY DECREASED RIGHT LOWER LOBE	SOFT, HEPATOMEGALY AND SPLENOMEGALY	S1 S2 HEARD	NORMAL	68.5	5.1	68			0.62	0.17	32	28	72	0.73	138	4.05	104	9
4	1440881	MS	B/L BASAL CREPTS	SOFT, NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	130	4.5	38			6.4	5.2	140	112	113	2.4	142	5.2	112	8.3
5	1427309	MS	RIGHT LOWER LOBE CREPTS	SOFT, NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	98.9	9.8	66	15.3	1.4	0.73	0.18	17	12	66	0.89	139	3.92	102	9.5
6	1436038	AS	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	1.8	120	12.5	11.8	1.08	0.39	0.22	16	16	60	0.85	140	4.07	103	
7	1469309	VS	B/L BASILAR CREPTS	SOFT, NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	0.8	7	12	15.2	1.4	0.4	0.12	45	42	36	0.93	142	3.2	122	
8	1431820	KLS	NVBS	SOFT, NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	9.1	5	16			0.61	0.15	16	224	114	0.84	138	3.96	105	9.6
9	1452305	JS	NVBS	SOFT, NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	14.5	3.8	80	14.6	1.34	0.34	0.08	17	42	53	0.78	137	4.4	107	7.5
10	1480877	SB	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	GCS- E1V1M1	23.9	4.3	8	17.2	1.54	0.83	0.35	14	9	42	0.69	136	3.87	104	9.6
11	1462145	GS	B/L BASILAR CREPTS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	0.98	5.8	9	14.5	1.33	0.66	0.12	20	99	96	0.6	135	3.6	101	
12	1486200	SV	NVBS	SOFT , SPLENOMEGALY	S1 S2 HEARD	NORMAL	54.5	7.8	70	13.7	1.25	0.53	0.07	37	45	23	0.79	133	4.56	94	
13	1471380	KK	BRONCHIAL BREATHING RIGHT SUBSCAPULAR REGION	SOFT ,NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	6.8	8.1	35	12.4	1.14	0.33	0.15	14	24	71	1.21	137	4.39	104	11.1
14	1487384	NR	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	21.1	6.9	52	24.2	2.25	0.59	0.7	10	8	52	1.46	134	6.21	105	8.2
15	1498895	BS	DECREASE AIR ENTRY LEFT SIDE	SOFT , NON TENDER , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	1.2	9.6	21	16.4	1.5	1.22	0.59	88	81	102	1.08	133	4.8	103	7.16
16	1505569	NB	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	28	7.7	40	13.4	1.23	0.52	0.11	12	23	62	0.49	136	4.27	95	8.3
17	1511450	KK	RIGHT UPPER LOBE -BRONCHIAL BREATHING	SOFT,NON TENDER	S1 S2 HEARD	NORMAL	1.85	6.3	130	13.9	1.27	0.52	0.1	28	21	61	0.79	141	4.3	107	
18	1498893	RS	NVBS	HEPATOSPLENOMEGALY	S1 S2 HEARD	NORMAL	40.5	6.4	36	16.6	1.52	4.68	2.76	69	64	96	1.78	134	3.98	97	
19	1507011	SP	NVBS	SOFT ,NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	3.7	10.1	44	14.2	1.32	0.44	0.06	26	46	143	0.87	138	4.6	102	
20	1523474	GS	NVBS	SOFT ,NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	3.2	9.4	44	15.1	1.32	0.88	0.42	40	42	120	1.2	136	4.5	102	9.2
21	1489323	M	B/L BASAL CREPTS	SOFT ,NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	10.9	9.4	26	16.6	1.52	0.4	0.29	135	74	85	1.5	140	3.9	105	9.6

			INVESTIGATIONS						
S.No.	MRD NO	Intials	MAGNESIUM	PHOSPHORUS	VIRAL MARKERS	CHEST XRAY	USG W/A	NCCT HEAD	HRCT CHEST
1	1452904	CL	2.13	2.7	NON REACTIVE	B/L LOWER ZONE HAZINESS	B/L RPC , HEPATOSPENOMEGALY	-	-
2	1461789	UJ	1.96	4.5	NON REACTIVE	INCREASE BRONCHOVASCULAR MARKING	HEPATOSPENOMEGALY , CHOLELITHIASIS	-	FLUID OVERLOAD WITH SUPERADDED INFECTION
3	1433542	HK	-	-	NON REACTIVE	LEFT COSTOPHRENIC ANGLE BLUNTING	HEPATOSPENOMEGALY , B/L PLEURAL EFFUSION	-	MILD LEFT PLEURAL EFFUSION WITH MINIMAL PERICARDIAL EFFUSION
4	1440881	MS	2.6	3.6	NON REACTIVE	NORMAL	NO SIGNIFICANT ABNORMALITY	-	-
5	1427309	MS	1.83	1.95	NON REACTIVE	RIGHT MIDDLE LOBE PATCH	HEAPTOMEGALY WITH FATTY LIVER GRAE II	-	PATCHY CONSOLIDATION WITH GROUND GLASS HAZE IN RIGHT MIDDLE LOBE
6	1436038	AS	-	-	NON REACTIVE	NORMAL	NO SIGNIFICANT ABNORMALITY	-	NO SIGNIFICANT ABNORMALITY
7	1469309	VS	-	-	NON REACTIVE	B/L RETICULONODULAR OPACITIES	NO SIGNIFICANT ABNORMALITY	-	-
8	1431820	KLS	2.1	2.6	NON REACTIVE	NORMAL	NO SIGNIFICANT ABNORMALITY	-	NO SIGNIFICANT ABNORMALITY
9	1452305	JS	2.6	2.17	NON REACTIVE	B/L FLUFFY SHADOWS PRESENT	SMALL COLLECTION IN PERINEUM	-	-
10	1480877	SB	1.96	3.9	NON REACTIVE	NORMAL		IPH WITH IVH WITH MIDLINE SHIFT	-
11	1462145	GS	-	2.05	NON REACTIVE	B/L BASAL HAZINESS	NO SIGNIFICANT ABNORMALITY	-	MULTIPLE B/LAIR SPACE NODULES ?INFECTIVE ?LYMPHOCYTIC INFILTRATION
12	1486200	SV	-	-	NON REACTIVE	NORMAL	LIVER HAEMANGIOMA , SPENOMEGALY	-	NO SIGNIFICANT ABNORMALITY
13	1471380	KK	-	-	NON REACTIVE	INCREASE BRONCHOVASCULAR MARKING	SMALL LEFT KIDNEY WITH RPC GRADE III	-	SUBCENTRIMETER NODULES IN BOTH LUNGS-?INFECTIVE
14	1487384	NR	5	1.74	NON REACTIVE	LEFT UPPER LOBE PATCH	MILD HEPATOMEGALY	-	FOCAL AREA OF CONSOLIDATIONLEFT UPPER LOBE
15	1498895	BS	-	1.85	NON REACTIVE	ARDS	HEAPTOMEGALY WITH PROSTATOMEGALY II	-	B/L LUNGS HYPERINFLATED,ARAEA OF CONSOLIDATION WITH CAVITATION LEFT LOWER LOBE
16	1505569	NB	1.6	3.1	NON REACTIVE	LEFT LOWER HAZINESS	HEPATOSPLENOMEGALY	-	LOBAR CONSOLIDATION OF LEFT LOWER LOBE WITH AIR BRONCHOGRAM-? FUNGAL
17	1511450	KK	-	-	NON REACTIVE	PATCH PRESENT RIGHT UPPER LOBE	NO SIGNIFICANT ABNORMALITY	-	INFECTIOUS BRONCHIOLOITIS RIGHT UPPER LOBE - ?FUNGAL
18	1498893	RS	-	-	NON REACTIVE	NORMAL	HEPATOSPLENOMEGALY	-	MINIMAL RIGHT PLEURAL EFFUSION
19	1507011	SP	-	-	NON REACTIVE	NORMAL	PROSTATOMEGALY	-	-
20	1523474	GS	1.8	2.4	NON REACTIVE	B/L PLEURAL EFFUSION		-	MILDB/LPLEURAL EFFUSION WITH UNDERLYING COLLAPSE/CONSOLIDATION
21	1489323	M	1.43	2.8	NON REACTIVE	B/L MODERATE PLEURAL EFFUSION ,B/L BASILAR CONSOLIDATION	MILD LEFT SIDED HYDRONEPHROSIS	-	B/L GGO - ? INFECTIVE ,B/L MODERATE PLEURAL EFFUSION

S.No.	MRD NO	Intials	2D ECHO	BONE MARROW ASPIRATION	BM ASPIRATE MUTATION	FLOWCYTOMETRY	BONE MARROW BIOPSY	PERIPHERAL BLOOD FLOWMETRY
1	1452904	CL	NORMAL LVEF=60 %	AML	NPM-1 AND FLT 3	-	AML-M5	-
2	1461789	UJ	NORMAL LVEF=60 %	ACUTE LEUKEMIA	NPM-1	HLA DR ,CD13,CD33,CD14,CD64,CD113	AML-M4	-
3	1433542	HK	NORMAL LVEF=60 %	ACUTE LEUKEMIA	AML PANEL NEGATIVE	HLA DR , CD34,CD117,CD 33,CD38 ,CD 123 -AML	AML-M3	-
4	1440881	MS	NORMAL LVEF=60 %	PRESENCE OF BLASTS CONSTITUTING 92 % OF ALL NUCLEATED CELLS	-	AML-M4	AML- M4	-
5	1427309	MS	NORMAL LVEF=60 %	AML	NPM-1 ,FLT -3	CD 117,CD13,CD33,CD38,CD123-AML	AML -M1	-
6	1436038	AS	NORMAL LVEF=60 %	PRESENCE OF BLAST CONSTITUTING 80% OF NUCLEATED CELLS	-	HLA DR,CD34,CD117,CD13,CD33,CD38,MPO- AML	AML- M2	-
7	1469309	VS	-	PRESENCE OF BLASTS CONSTITUTING 40% OF ALL NUCLEATED CELLS	-		AML - M4	-
8	1431820	KLS	-	PRESENCE OF BLAST CONSTITUTING 40% OF NUCLEATED CELLS, AUER RODS PRESENT	-	HLA DR ,CD34,CD117,CD13,CD33,MPO-AML	AML-M2	-
9	1452305	JS	NORMAL LVEF=60 %	PRESENCE OF BLASTS CONSTITUTING 88% OF ALL NUCLEATED CELLS -AML	-	CD113,CD13,CD33,MPO,CD123-AML	AML-M1	-
10	1480877	SB	NORMAL LVEF=60 %	APML	-	CD34,CD117,CD13,CD33,CD64,MPO-APML	APML-M3	-
11	1462145	GS	-	AML POSSIBLY APML	PML-RARA,FLT3-D835,FLT3-ITD	CD117,CD13,CD33,CD64,CD38,MPO,CD123-APML	APML-M3	-
12	1486200	SV	MILD CONCENTRIC LVH WITH LVEF=60%	PRESENCE OF BLASTS CONSTITUTING 90% OF ALL NUCLEATED CELLS	-	HLA DR,CD13,CD33,CD14,CD64,CD38-AML WITH MONOCYTIC DIFFERENTIATION	AML-M4	-
13	1471380	KK	NORMAL LVEF=60 %	PRESENCE OF BLASTS CONSTITUTING 95 % OF ALL NUCLEATED CELLS	-	AML	AML-M0/M1	-
14	1487384	NR	NORMAL LVEF=60 %	PRESENCE OF BLASTS CONSTITUTING 90% OF ALL NUCLEATED CELLS	AML PANEL NEGATIVE	AML	AML-M0/M1	-
15	1498895	BS	-	ACUTE LEUKEMIA	-	HLA DR,CD34,CD117,CD13,CD33,CD64,CD38-AML	AML-M0/M1	-
16	1505569	NB	NORMAL LVEF=60 %	-	AML PANEL NEGATIVE	-	AML-M0/M1	HLADR,CD 34,CD117,CD13,CD 123 -AML
17	1511450	KK	NORMAL LVEF=60 %	PRESENCE OF BLASTS CONSTITUTING 44% OF ALL NUCLEATED CELLS	-	HLA DR ,CD117,CD13,CD33,CD38-AML	AML-M2	-
18	1498893	RS	GHK WITH LVEF=46%	PRESENCE OF BLASTS CONSTITUTING 80% OF ALL NUCLEATED CELLS -AML	-	HLA DR,CD34,CD117,CD13,CD33,CD38-AML	AML-M0/M1	-
19	1507011	SP	-	MATURATION ARREST WITH PROMINENCE OF MYELOCYTE AND METAMYELOCYTES WITH>10% BLASTS	-	HLA DR,CD34,CD117,CD13,CD33,CD38,CD123-AML WITH MONOCYTIC DIFFERENTATION	AML-M4	-
20	1523474	GS	-	-	-		AML-M5	HLA DR ,CD13,CD14,CD117,CD38,CD123-AML WITH MONOCYTIC MATURATION
21	1489323	M	NORMAL LVEF=60%	PROMINENCE OF ATYPICAL PROMYELOCYTE CONSTITUTING 90% OF ALL NUCLEATED CELLS	PML-RARA	CD 117,CD 13, CD 33,CD 14, CD 64 , CD 38, MPO, CD 123 =APML	APML-M3	-

			FINAL DIAGNOSIS	TREATMENT						
S.No.	MRD NO	Intials		STARTED - YES/NO	HYPOMETHYLATING AGENTS (AZACYTIDINE,DECITABINE)	HYPOMETHYLATING AGENTS WITH VENETOCLAX	INTENSIVE CHEMOTHERAPY	PALLIATION	MEDICAL MANAGEMENT (ANTIBIOTICS)	EMPIRICAL ANTIFUNGALS STARTED
1	1452904	CL	AML WITH LRTI WITH AKI	YES	AZACYTIDINE	-	-	-	YES	YES -MICAFUNGIN
2	1461789	UJ	AML M4 WITH SEVERE ANEMIA	YES	AZACYTIDINE	-	-	-	YES	POSACONAZOLE
3	1433542	HK	APML	YES	ATO AND ATRA	-	-	-	YES	AMPHOTERICIN
4	1440881	MS	AML WITH LRTI SEPSIS WITH SEPTIC SHOCK	NO	-	-	-	-	YES	VORICONAZOLE
5	1427309	MS	AML WITH LRTI	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
6	1436038	AS	AML	YES	CYTARABINE PLUS DAUNORUBICIN	-	-	-	YES	VORICONAZOLE
7	1469309	VS	AML WITH LRTI SEPSIS WITH SEPTIC SHOCK WITH RESPIRSTORY FAILURE	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
8	1431820	KLS	AML	YES	CYTARABINE PLUS DAUNORUBICIN	-	-	-	YES	POSACONAZOLE
9	1452305	JS	AML	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
10	1480877	SB	APML WITH ICH WITH SEPSIS WITH SEPTIC SHOCK	NO	-	-	-	-	YES	VORICONAZOLE
11	1462145	GS	APML WITH LRTI SEPSIS-FUNGAL	YES	-	-	ATO,ATRA	-	YES	POSACONAZOLE
12	1486200	SV	AML-M4	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	POSACONAZOLE
13	1471380	KK	LRTI SEPSIS	YES	AZACYTIDINE		-	-	YES	POSACONAZOLE
14	1487384	NR	AML WITH LRTI SEPSIS	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
15	1498895	BS	AML WITH LRTISEPSIS	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	POSACONAZOLE
16	1505569	NB	AML WITH LRTI SEPSIS	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
17	1511450	KK	AML WITH LRTI SEPSIS- ?FUNGAL	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
18	1498893	RS	AML WITH LRTI WITH AKI WITH HYPERBILIRUBINEMIA	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	POSACONAZOLE
19	1507011	SP	HYPERTENSION, AML-M4 WITH PANCYTOPENIA	YES	AZACYTIDINE	-	-	-	YES	POSACONAZOLE
20	1523474	GS	DM2,HYPERTENSION ,AML-M5	NO	-	-	-	-	YES	-
21	1489323	M	APML, LRTI SEPSIS , MILD LEFT HYDRONEPHROSIS,AKI	YES	-	-	ATO,ATRA	-	YES	VORICONAZOLE

			LENGTH OF HOSPITAL STAY	COMPLETE REMISSION YES/NO		FINAL OUTCOME				SATUS @ FOLLOWUP (AFETR 3MONTHS)	STATUS ON LAST FOLLOW UP(ALIVE/DIED)	
S.No.	**MRD NO**	**Intials**	**LENGTH OF HOSPITAL STAY**	**COMPLETE REMISSION YES/NO**	**ON BONE MARROW REMISSION**	**DISCHARGED**	**DISCHARGED ON REQUEST**	**DAMA**	**EXPIRED**			**SURVIVAL DAYS**
1	1452904	CL	4 DAYS	-	-	-	-	Yes	-	DIED	28/2/23 (DIED)	32
2	1461789	UJ	6 DAYS	-	-	Yes	-	-	-	LOST TO FOLLOWUP	18/2/23(LOST TO FOLLOWUP)	36
3	1433542	HK	14 DAYS	YES	90 TH DAY	Yes	-	-	-	HEALTHY	JAN 2024 (DIED)	389
4	1440881	MS	15 DAYS	-	-	-	-	-	Yes	DIED	DIED	17
5	1427309	MS	27 DAYS	YES	30 TH DAY	Yes	-	-	-	HEALTHY	FEB 2023 (DIED)	64
6	1436038	AS	26 DAYS	YES	14 TH DAY	Yes	-	-	-	HEALTHY	JUNE 2024 (DIED)	162
7	1469309	VS	5 DAYS	-	-	-	-	Yes	-	DIED	DIED	10
8	1431820	KLS	31 DAYS	YES	14TH DAY	Yes	-	-	-	HEALTHY	MAY 2024 (DIED)	885
9	1452305	JS	14 DAYS	YES	60 TH DAY	Yes	-	-	-	DIED	DIED	61
10	1480877	SB	3 DAYS	-	-	-	-	Yes	-	DIED	DIED	4
11	1462145	GS	10 DAYS	YES	60TH DAY	Yes	-	-	-	HEALTHY	SEP 2023 (ALIVE)	380
12	1486200	SV	3 DAYS	-	-	Yes	-	-	-	HEALTHY	MAR 2024 (ALIVE)	342
13	1471380	KK	24 DAYS	-	-	-	-	Yes	-	EXPIRED	APRIL 2023 (DIED)	38
14	1487384	NR	8 DAYS	-	-	Yes	-	-	-	LOST TO FOLLOWUP	LOST TO FOLLOW UP	30
15	1498895	BS	9 DAYS	-	-	Yes	-	-	-	DIED	MAY 2023 (DIED)	34
16	1505569	NB	4 DAYS	-	-	Yes	-	-	-	HEALTHY	SEP 2023 (DIED)	156
17	1511450	KK	12 DAYS	YES	90 TH DAY	Yes	-	-	-	HEALTHY	DEC 2023 (ALIVE)	318
18	1498893	RS	12 DAYS	NO	-	-	-	Yes	-	RELAPSE	JULY 2023 (DIED)	100
19	1507011	SP	12 DAYS	-	-	Yes	-	-	-	HEALTHY	JAN 2024 (ALIVE)	297
20	1523474	GS	7 DAYS	-	-	-	-	Yes	-	DIED	JUNE 2023 (DIED)	33
21	1489323	M	24 DAYS	YES	60TH DAY	Yes	-	-	-	HEALTHY	NOV 2023 (ALIVE)	338

							CHIEF COMPLAINTS						GENERAL EXAMINATION							
S.No.	MRD NO	Intials	AGE (Years)	SEX	DATE OF ADMISSION	DATE OF DIAGNOSIS	FEVER	COUGH	SHORTNESS OF BREATH	ALTERED SENSORIUM	GENERALISED WEAKNESS	BLEEDING MANIFESTATION	PALLOR	ICTERUS	Spo2 (%)	HEART RATE(BPM)	RESP RATE (PER MIN)	SBP(mmhg)	DBP(mmhg)	BODY TEMP(f)
22	1493133	PK	40	FEMALE	4/5/2023	4-Apr	YES	NO	NO	NO	YES	-	YES	NO	96	96	16	112	88	98
23	1423826	JKC	71	MALE	4/29/2023	4/6/2023	YES	YES	YES	NO	NO	-	NO	NO	98	78	25	120	70	98.9
24	1592291	AS	28	FEMALE	9/18/2023	9/20/2023	YES	YES	NO	NO	NO	-	NO	NO	98	112	26	100	70	98.9
25	1500450	KK	60	FEMALE	4/17/2023	4/18/2023	NO	NO	NO	NO	YES	-	YES	NO	98	78	16	10	83	99
26	1574565	RK	51	FEMALE	8/21/2023	9/23/2023	YES	NO	NO	NO	NO	YES (LOWER GI BLEED)	NO	NO	96	117	18	148	88	98
27	1584866	SP	74	MALE	9/8/2023	9/8/2023	YES	NO	NO	NO	NO	-	NO	NO	99	86	20	110	70	98
28	1570050	MK	30	FEMALE	8/12/2023	8/14/2023	YES	NO	NO	NO	NO	-	NO	NO	99	86	20	117	82	98.8
29	1632029	VK	72	MALE	12/12/2023	12/14/2023	YES	NO	NO	NO	NO	-	YES	NO	98	112	28	110	70	99
30	1637186	BK	65	FEMALE	12/11/2023	12/14/2023	YES	YES	YES	NO	NO	-	NO	NO	98	75	14	114	80	99
31	1664146	GSD	73	MALE	3/2/2024	3/4/2024	YES	NO	NO	NO	NO	YES (SUBDURAL HEMATOMA)	NO	NO	98	68	18	135	4.07	102
32	1625942	GKS	72	FEMALE	11/23/2023	11/26/2023	YES	NO	NO	NO	NO	-	NO	NO	98	78	20	140	90	98
33	1680072	VD	66	FEMALE	2/24/2024	2/25/2024	YES	NO	NO	NO	NO	YES (MALENA)	NO	NO	95	134	26	130	90	99
34	1682887	HOS	65	MALE	2/28/2024	2/29/2024	YES	YES	YES	NO	NO	-	YES	NO	99	98	22	110	70	98
35	1469769	JK	71	FEMALE	2/24/2023	2/26/2023	YES	YES	NO	NO	NO	-	YES	NO	99	142	26	90	60	99
36	1546923	MK	66	FEMALE	7/4/2023	7/6/2023	YES	NO	NO	NO	NO	-	YES	NO	96	89	18	110	90	98
37	1480640	SK	43	FEMALE	4/16/2023	4/17/2023	YES	NO	NO	NO	YES	-	NO	NO	98	98	22	120	76	97
38	1490683	MS	51	MALE	3/31/2023	4/3/2023	NO	NO	NO	NO	YES	-	NO	NO	97	98	16	110	70	98
39	1497595	BK	60	FEMALE	4/11/2023	4/12/2023	NO	NO	NO	NO	YES	-	YES	NO	98	114	20	118	88	98
40	1486633	R	27	MALE	3/24/2023	3/24/2023	YES	NO	NO	NO	YES	YES (INTRAPARENCHYMAL HAEMOORHAGE)	YES	NO	98	126	28	110	70	99
41	1449815	NSN	41	MALE	1/22/2023	1/26/2023	YES	NO	NO	NO	NO	YES(GUM BLEEDING)	YES	NO	98	112	26	110	70	98

			SYSTEMIC EXAMINATION																		
S.No.	MRD NO	Intials	RESPIRATORY	ABDOMEN	CVS	CNS	TLC	HB	PLATELET	PTI	INR	BIL (t)	BIL(d)	SGOT	SGPT	ALP	CREATININE	Na	K	Cl	Calcium
22	1493133	PK	BRONCHIAL BREATHINGPRESENT RIGHT SUBSCAPULAR REGION	SOFT,NO PALPABLE ORGANOMEGLY	S1 S2 HEARD	NORMAL	10.7	5.1	40	17.4	1.32	0.32	0.16	26	11	78	0.74	132	3.8	95	7.2
23	1423826	JKC	B/L BASAL CREPTS	SOFT, NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	23	704	62			0.5	0.09	13	28	65	0.83	132	4.2	100	9.2
24	1592291	AS	B/L BASAL CREPTS	SOFT,HEPATOMEGALY, SPLENOMEGALY	S1 S2 HEARD	NORMAL	1.5	8.4	82	13.4	1.4	0.56	0.14	21	23	51	0.51	136	4.5	95	8.5
25	1500450	KK	NVBS	SOFT,NO PALPABLE ORGANOMEGLY	S1 S2 HEARD	NORMAL	1.77	6.3	130	13.7	1.28	0.52	0.1	24	21	61	0.72	141	4.3	107	
26	1574565	RK	NVBS	SOFT ,NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	1.3	7.5	42	17.2	1.2	0.8	0.02	46	82	96	0.64	136	3.8	100	8.4
27	1584866	SP	B/L FINE CREPTS	SOFT ,NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	135	5.5	12	17.2	1.23	0.6	0.2	22	20	48	0.7	135	3.3	95	
28	1570050	MK	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	45.9	9.7	60	16.7	1.23	0.53	0.11	23	22	108	0.69	137	4.4	105	
29	1632029	VK	B/L CREPTS	SOFT ,NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	117.5	4.9	132	17	1.4	0.77	0.21	48	26	65	0.95	133	4.3	96	8.2
30	1637186	BK	B/L BASAL CREPTS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	37.7	7	210	13.7	1.25	0.56	0.56	0.29	18	11	0.4	118	3.27	84	8.2
31	1664146	GSD	B/L FINE CREPTS	SOFT ,NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	26.7	8.9	14	19.7	1.8	0.92	0.19	43	33	78	0.86	135	4.07	102	9.2
32	1625942	GKS	NVBS	SOFT,NO PALPABLE ORGANOMEGLY	S1 S2 HEARD	NORMAL	10.1	10.2	60	14.2	1.24	0.66	0.07	38	53	108	0.66	126	4.14	83	9.68
33	1680072	VD	B/L BASAL CREPTS	SOFT , SPLENOMEGALY	S1 S2 HEARD	NORMAL	1.4	8.3	10	19.9	1.81	0.48	0.82	13	41	84	0.91	132	4.1	98	
34	1682887	HOS	B/L BASAL CREPTS	SOFT,SPLENOMEGALY	S1 S2 HEARD	NORMAL	3.2	6.4	16	17.2	1.5	0.57	0.02	23	22	82	0.87	133	5.43	106	
35	1469769	JK	B/L DIFFUSE COARSE CREPTS	SOFT , DISTENDED	S1 S2 HEARD	NORMAL	23.2	7	10	17.8	1.63	0.88	0.32	46	16	58	1.18	141	3.18	109	8.2
36	1546923	MK	NVBS	SPLENOMEGALY	S1 S2 HEARD	NORMAL	21.9	7.7	617	14.1	1.3	0.5	0.23	21	11	215	0.71	144	4.3	112	
37	1480640	SK	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	34.8	7.9	8	16.2	1.3	0.42	0.1	30	45	58	1.17	137	3.8	103	8.4
38	1490683	MS	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	275	4.8	22	19.9	1.81	0.44	0.06	26	40	143	0.87	138	4.6	102	8.1
39	1497595	BK	BRONCHIAL BREATHING LEFT UPPER LOBE	SOFT ,HEPATOSPLENOMEGALY	S1 S2 HEARD	NORMAL	55	4.4	26	13.4	1.23	0.52	0.11	12	23	84	0.63	135	4.5	99	8.8
40	1486633	R	B/L CREPTS IN ALL LOBES	SOFT, HEPATOMEGALY AND SPLENOMEGALY	S1 S2 HEARD	NORMAL	9.85	7.6	14			0.69	0.17	25	19	60	2.32	134	3.53	98	7.7
41	1449815	NSN	B/L CREPTS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	34.7	7.7	40	15.2	1.39	0.3	0.13	25	28	138	0.83	136	4.03	102	8.2

			INVESTIGATIONS						
S.No.	MRD NO	Intials	MAGNESIUM	PHOSPHORUS	VIRAL MARKERS	CHEST XRAY	USG W/A	NCCT HEAD	HRCT CHEST
22	1493133	PK	2.92	3.2	NON REACTIVE	B/L LOWER ZONE HAZINESS		-	BRONCHITIS WITH AIR TRAPPING
23	1423826	JKC	2.03	2.5	NON REACTIVE	RETICULATIONS IN B/L LOWER LOBES		-	-
24	1592291	AS	2.48	2.21	NON REACTIVE	B/L INFILTRATES	HEPATOSPLENOMEGALY	-	MULTIFOCAL GROUND GLASS OPACITIES IN B/L LUNGS - ?VIRAL
25	1500450	KK	-	-	NON REACTIVE	PATCH PRESENT RIGHT UPPER LOBE		-	INFECTIOUS BRONCHIOLOITIS RIGHT UPPER LOBE - ?FUNGAL
26	1574565	RK	1.4	2.9	NON REACTIVE	INCREASE BRONCHOVASCULAR MARKING	ILEOCOLIC MESENTRIC LYMPHADENOPATHY	-	VOLUME OVERLOAD WITH SUPERADDED INFECTION
27	1584866	SP	-	-	NON REACTIVE	B/L INCREASED BRONCHOVASCULAR MARKING	NO SIGNIFICANT ABNORMALITY	-	VOLUME OVERLOAD WITH SUPERADDED INFECTION
28	1570050	MK	-	-	NON REACTIVE	NORMAL	NO SIGNIFICANT ABNORMALITY	-	-
29	1632029	VK	2.6	1.9	NON REACTIVE	B/L HAZINESS	NO SIGNIFICANT ABNORMALITY	-	-
30	1637186	BK	2.41	3.63	NON REACTIVE	INCREASE BRONCHOVASCULAR MARKING	B/L RPC GRADE 1 , MINIMAL LEFT PLEURAL EFFUSION	-	FLUID OVERLOAD WITH SUPERADDED INFECTION
31	1664146	GSD	2.6	2.9	NON REACTIVE	B/L HETEROGENOUS OPACITIES	NO SIGNIFICANT ABNORMALITY	-	ORGANISING PNEUMONIA -?VIRAL
32	1625942	GKS	2.6	3.9	NON REACTIVE		NO SIGNIFICANT ABNORMALITY	-	-
33	1680072	VD	-	-	NON REACTIVE	NORMAL	SPLENOMEGALY, B/L RPC GRADE I	-	-
34	1682887	HOS	-	-	NON REACTIVE	B/L HOMOGENOUS OPACITIES	NO SIGNIFICANT ABNORMALITY	-	EXTENSIVE AREA OF GROUNG GLASS HAZE WITH SEPTAL THICKENING
35	1469769	JK	1.77	2.3	NON REACTIVE	DIFFUSE OPACITIES	FATTY LIVER GRADE-I	-	FUNGAL PNEUMONIA
36	1546923	MK	-	-	NON REACTIVE	NORMAL	MASSIVE SPLENOMEGALY, HEPATOMEGALY	-	-
37	1480640	SK	4.3	1.83	NON REACTIVE	B/L LOWER ZONE HAZINESS	FATTY LIVER GRADE-I	-	-
38	1490683	MS	2.6	1.92	NON REACTIVE	NORMAL	PROSTATOMEGALY	-	-
39	1497595	BK	3.6	1.6	NON REACTIVE	LEFT UPPER LOBE CONSOLIDATION	HEPATOSPLENOMEGALY	-	FUNGAL PNEUMONIA
40	1486633	R	2.7	1.97	NON REACTIVE	NORMAL	FATTY LIVER GRADE-II	IPH WITH SDH,SAH	-
41	1449815	NSN	3.9	2	NON REACTIVE	B/L INFILTRATES		-	FEW MILLIMETRIC SCATTERED SOLID NODULES - ? LEUKEMIC INFILTRATES

S.No.	**MRD NO**	**Intials**	**2D ECHO**	**BONE MARROW ASPIRATION**	**BM ASPIRATE MUTATION**	**FLOWCYTOMETRY**	**BONE MARROW BIOPSY**	**PERIPHERAL BLOOD FLOWMETRY**
22	1493133	PK	NORMAL LVEF=60%	AML	-	HLA DR ,CD34,CD117,CD13,CD33,MPO-AML	AML-M2	-
23	1423826	JKC	NORMAL LVEF=60%	-	-	-	(PERIPHERAL BLOOD - M2)	HLA DR, CD 34,CD117,CD13,CD33,CD38,MPO,CD123-AML M2
24	1592291	AS	NORMAL LVEF=60%	PRESENCE OF BLASTS CONSTITUTING 40 %OF ALL NUCLEATED CELLS- HEMATOLYMPHOID MALIGNANCY	-	CD 117,CD13,CD33,CD64,CD38,MPO -AML	AML- M3	-
25	1500450	KK	NORMAL LVEF=60%	PRESENCE OF BLASTS CONSTITUTING 44 %OF ALL NUCLEATED CELLS- ACUTE LEUKEMIA	-	HLA DR,CD117,CD13,CD33,CD38,CD123-AML	AML-M0/M1	-
26	1574565	RK	-	PRESENCE OF BLASTS CONSTITUTING 96 % OF ALL NUCLEATED CELLS -AML	NPM1,FLT3-ITD	HLA DR,CD117,CD13,CD33,CD38,CD 7,MPO-AML	AML-M2	-
27	1584866	SP	NORMAL LVEF=60%	HYPERCELLULAR MARROW WITH PRESENCE OF 95 % BLASTS	CBFB-MYH11	HLA DR ,CD34,CD 117,CD 13,-AML WITH MONOCYTIC DIFFERENTATION	AML-M4	-
28	1570050	MK	NORMAL LVEF=60%	PRESENCE OF BLASTS CONSTITUTING 76% OF ALL NUCLEATED CELLS -AML	-	HLA DR,CD 34,CD117,CD13,CD33,CD64,CD10,CD38-AML	AML-M2	-
29	1632029	VK	NORMAL LVEF=60%	AML	-	HLA DR,CD117,CD13,CD33,CD38,CD 7,MPO-AML	AML-M2	-
30	1637186	BK	NORMAL LVEF=60%	PRESENCE OF BLASTS CONSTITUTING 80% OF ALL NUCLEATED CELLS -AML	NPM 1	HLA DR,CD34,CD117,CD33,CD 13,CD 38, CD123 - AML WITH MONOCYTIC DIFFERENTATION	AML -M4	-
31	1664146	GSD	NORMAL LVEF=60%	-	PML-RARA ,FLT3-ITD	-	APML-M3	CD34,CD117,CD 13,CD33,CD64,MPO-AML
32	1625942	GKS	NORMAL LVEF=60%	ACUTE LEUKEMIA	AML PANEL NEGATIVE	CD 117,CD13,CD33,CD64,CD7,CD38, MPO-AML	AML-M2	-
33	1680072	VD	-	-	-	-	AML-M1	CD34,CD117,CD 13,CD33,CD10,CD38,CD123-AML
34	1682887	HOS	NORMAL LVEF=60%	AML	AML PANEL NEGATIVE	HLA DR ,CD34,CD 117,CD 13,-AML WITH MONOCYTIC DIFFERENTATION	AML-M4	-
35	1469769	JK	NORMAL LVEF=60%	PROMINENCE OF BLASTS AND ATYPICAL PROMYELOCYTES CONSTITUTING 90 % OF ALL NUCLEATED CELLS	-	-	APML-M3	-
36	1546923	MK	NORMAL LVEF=60%	BLASTS CONSTITUTING 20% OF ALL NUCLEATED CELLS	-	HLA DR, CD 34,CD 117,CD 13,CD38,CD123-AML	AML-M4	-
37	1480640	SK	NORMAL LVEF=60%	PRESENCE OF BLASTS CONSTITUTING 90% OF ALL NUCLEATED CELLS	-	HLA DR,CD 123,CD117,CD13,CD38,MPO-AML	AML-M2	-
38	1490683	MS	NORMAL LVEF=60%	PRESENCE OF BLASTS CONSTITUTING 30 % OF ALL NUCLEATED CELLS AND ATYPICAL MONOCYTOID CELLS	-	HLA DR,CD34,CD117,CD13,CD33,CD38,CD123-AML WITH MONOCYTIC DIFFERENTATION	AML-M4	-
39	1497595	BK	NORMAL LVEF=60%	PRSENCE OF BLASTS CONSTITUING 65 % OF ALL NUCLEATED CELLS	-	HLA DR ,CD 34,CD117,CD13,CD33 ,CD 38,CD123	AML-M2	-
40	1486633	R	NORMAL LVEF=60%	PROMINENCE OF ATYPICAL MONOCYTOID CELLS CONSTITUTING 85% OF ALL NUCLEATED CELLS-AML	-	CD 117,CD 13, CD 33,CD 14, CD 64 , CD 38, MPO, CD 123 =APML	APML-M3	-
41	1449815	NSN	NORMAL LVEF=60%	-	-	-	APML-M3	CD117,CD13,CD33.CD64,CD38,MPO,CD123-APML

			FINAL DIAGNOSIS	TREATMENT						
S.No.	MRD NO	Intials		STARTED - YES/NO	HYPOMETHYLATING AGENTS (AZACYTIDINE,DECITABINE)	HYPOMETHYLATING AGENTS WITH VENETOCLAX	INTENSIVE CHEMOTHERAPY	PALLIATION	MEDICAL MANAGEMENT (ANTIBIOTICS)	EMPIRICAL ANTIFUNGALS STARTED
22	1493133	PK	AMLWITH LTRI SEPSIS ? FUNGAL	YES	AZACYTIDINE	-	-	-	YES	POSACONAZOLE
23	1423826	JKC	COPD WITH AML-M2 WITH NEUTOPENIC SEPSIS WITH LRTI ,UTI SEPSIS WITH SEPTIC SHOCK	NO	-	-	-	-	YES	VORICONAZOLE
24	1592291	AS	AML-M 3 WITH LRTI ?VIRAL	YES	-	-	ATO,ATRA	-	YES	POSACONAZOLE
25	1500450	KK	AML WITH AMTURATION WITH LRTI SEPIS - ?FUNGAL	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
26	1574565	RK	AML WITH LRTI WITH ILEAL ULCER	YES	CYTARABINE PLUS DAUNORUBICIN	-	-	-	YES	POSACONAZOLE
27	1584866	SP	AML -M4 WITH LRTI SEPSIS	YES	AZACYTIDINE	-	-	-	YES	POSACONAZOLE
28	1570050	MK	AML	YES	CYTARABINE PLUS DAUNORUBICIN	-	-	-	YES	POSACONAZOLE
29	1632029	VK	AML WITH LRTI SESPSIS WITH SEPTIC SHOCH WITH RESPIRATORY FAILURE	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	POSACONAZOLE
30	1637186	BK	AML WITH MONOCYTIC DIFFERENTIATION	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
31	1664146	GSD	APML WITH B/L SUBDURAL HAEMATOMA WITH FUNGAL PNEUMONIA WITH AKI	YES	-	-	ATO ,ATRA,MITOXANTRONE	-	YES	MICAFUNGIN
32	1625942	GKS	AML	YES	AZACYTIDINE	-	-	-	YES	POSACONAZOLE
33	1680072	VD	AML WITH LRTI SEPSIS WITH COAGULOPATYHY WITH GI BLEED	NO	-	-	-	-	YES	
34	1682887	HOS	AML WITH LRTI SEPSIS- ?FUNGAL	YES	AZACYTIDINE	-	-	-	YES	VORICONAZOLE
35	1469769	JK	T2DM,HYPERTENSION,CAD,APML	YES	-	-	ATO,ATRA	-	YES	VORICONAZOLE
36	1546923	MK	AML	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	POSACONAZOLE
37	1480640	SK	AML	NO	-	-	-	-	YES	-
38	1490683	MS	AML-M4	YES	AZACYTIDINE	-	-	-	YES	VORICONAZOLE
39	1497595	BK	AML WITH LRTI SEPSIS	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
40	1486633	R	APML WITH IPH	NO	-	-	-	-	YES	-
41	1449815	NSN	TYPE 2 DM, APML	YES	-	-	IDARUBICIN PLUS ATRA,ATO	-	YES	VORICONAZOLE

			LENGTH OF HOSPITAL STAY	COMPLETE REMISSION YES/NO		FINAL OUTCOME				SATUS @ FOLLOWUP (AFETR 3MONTHS)	STATUS ON LAST FOLLOW UP(ALIVE/DIED)	
S.No.	**MRD NO**	**Intials**	**LENGTH OF HOSPITAL STAY**	**COMPLETE REMISSION YES/NO**	**ON BONE MARROW REMISSION**	**DISCHARGED**	**DISCHARGED ON REQUEST**	**DAMA**	**EXPIRED**			**SURVIVAL DAYS**
22	1493133	PK	10 DAYS	YES	30TH DAY	Yes	-	-	-	HEALTHY	FEB 2024 (ALIVE)	312
23	1423826	JKC	9 DAYS	NO	-	-	-	-	Yes	DIED	APRIL 2023 (DIED)	323
24	1592291	AS	45 DAYS	YES	30TH DAY	Yes	-	-	-	HEALTHY	MAY 2024 (ALIVE)	250
25	1500450	KK	11 DAYS	YES	90TH DAY	Yes	-	-	-	HEALTHY	DEC 2023 (ALIVE)	254
26	1574565	RK	32 DAYS	YES	90TH DAY	Yes	-	-	-	HEALTHY	JAN 2024 (DIED)	129
27	1584866	SP	11 DAYS			Yes	-	-	-	HEALTHY	MAR 2024 (ALIVE0	175
28	1570050	MK	20DAYS	YES	30TH DAY	Yes	-	-	-	HEALTHY	LOST TO FOLLOW UP	122
29	1632029	VK	2 DAYS	-	-	-	-	Yes	-	DIED	DIED	2
30	1637186	BK	9 DAYS	-	-	Yes	-	-	-	LOST TO FOLLOWUP	LOST TO FOLLOW UP	14
31	1664146	GSD	30 DAYS	YES	30TH DAY	Yes	-	-	-	HEALTHY	MAY 2024 (ALIVE)	3
32	1625942	GKS	3 DAYS	-	-	-	-	Yes	-	DIED	DIED	4
33	1680072	VD	2 DAYS	-	-	-	-	Yes	-	DIED	DIED	3
34	1682887	HOS	7 DAYS	-	-	Yes	-	-	-	HEALTHY	MAY 2024 (ALIVE)	1
35	1469769	JK	3 DAYS	-	-	-	-	-	Yes	DIED	DIED	3
36	1546923	MK	4 DAYS	NO	-	Yes	-	-	-	RELAPSE	DIED	108
37	1480640	SK	5 DAYS	-	-	-	-	Yes	-	DIED	DIED	6
38	1490683	MS	6 DAYS	-	-	-	-	-	Yes	DIED	DIED	6
39	1497595	BK	10 DAYS	-	-	Yes	-	-	-	RELAPSE	AUG 2023 (DIED)	134
40	1486633	R	4 DAYS	-	-	-	-	Yes	-	DIED	DIED	6
41	1449815	NSN	14 DAYS	YES	90TH DAY	Yes	-	-	-	HEALTHY	DEC 2023 (ALIVE)	423

							CHIEF COMPLAINTS						GENERAL EXAMINATION							
S.No.	MRD NO	Intials	AGE (Years)	SEX	DATE OF ADMISSION	DATE OF DIAGNOSIS	FEVER	COUGH	SHORTNESS OF BREATH	ALTERED SENSORIUM	GENERALISED WEAKNESS	BLEEDING MANIFESTATION	PALLOR	ICTERUS	Spo2 (%)	HEART RATE(BPM)	RESP RATE (PER MIN)	SBP(mmhg)	DBP(mmhg)	BODY TEMP(f)
42	1661520	BS	56	MALE	1/30/2024	1/31/2024	YES	YES	NO	NO	NO	-	YES	NO	98	118	20	118	90	97
43	1660685	RD	53	MALE	1/28/2024	1/30/2024	NO	NO	NO	NO	YES	-	NO	NO	98	76	22	120	90	96
44	1655373	MK	38	FEMALE	1/18/2024	1/20/2024	YES	NO	NO	NO	YES	-	NO	NO	90	88	18	110	90	97
45	1631440	HK	31	FEMALE	11/30/2023	12/2/2023	YES	YES	NO	NO	NO	-	YES	NO	99	112	26	100	70	99
46	1441728	HS	69	MALE	1/4/2023	1/6/2023	YES	NO	NO	NO	YES	YES (GUM BLEEDING)	YES	NO	98	100	20	110	80	99
47	1163398	VS	46	MALE	8/29/2021	8/31/2021	YES	NO	NO	NO	YES	-	NO	NO	99	110	22	110	90	97
48	1686566	NS	57	MALE	3/5/2023	3/9/2023	YES	NO	NO	NO	YES	NASAL BLEEDING	YES	NO	99	101	18	120	90	98
49	1609698	HS	62	MALE	10/17/2023	10/18/2023	NO	NO	NO	NO	YES	-	YES	NO	99	88	23	100	70	99
50	1639264	GK	62	FEMALE	12/10/2023	12/13/2023	YES	YES	NO	NO	NO	-	YES	NO	98	66	18	140	90	98

			SYSTEMIC EXAMINATION																		
S.No.	MRD NO	Intials	RESPIRATORY	ABDOMEN	CVS	CNS	TLC	HB	PLATELET	PTI	INR	BIL (t)	BIL(d)	SGOT	SGPT	ALP	CREATININE	Na	K	Cl	Calcium
42	1661520	BS	RIGHT BASE COARSE CREPTS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	98	7	65	14.1	1.2	0.8	0.12	12	10	62	0.93	147	3.6	112	7.2
43	1660685	RD	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	23	8.6	221			0.88	0.07	25	12	53	0.86	142	3.9	102	
44	1655373	MK	B/L FINE CREPTS	SOFT , DISTENDED	S1 S2 HEARD	NORMAL	1.2	5.6	26	14.5	0.99	0.66	0.07	66	44	101	1.2	136	4.2	112	
45	1631440	HK	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	3	6	100	20	1.82	0.39	0.22	13	21	113	0.7	138	3.3	101	
46	1441728	HS	B/L CREPTS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	28.7	7	20			1.6	1.04	184	102	451	0.9	137	3.26	102	8
47	1163398	VS	NVBS	SOFT , NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	41.1	7.9	60	14.6	1.34	0.86	0.22	25	14	85	0.86	138	4.15	102	7.2
48	1686566	NS	NVBS	SOFT,NO PALPABLE ORGANOMEGLY	S1 S2 HEARD	NORMAL	1.1	6.8	225			0.82	0.45	17	21	119	0.75	134	4.4	99	
49	1609698	HS	NVBS	SOFT,NO PALPABLE ORGANOMEGLY	S1 S2 HEARD	NORMAL	66.9	5.6	150	14.9	1.4	0.59	0.2	10	7	119	0.66	133	4	104	
50	1639264	GK	NVBS	SOFT, NO PALPABLE ORGANOMEGALY	S1 S2 HEARD	NORMAL	1.9	3.3	18			0.99	0.51	8	14	71	1.11	138	4.75	104	

			INVESTIGATIONS						
S.No.	MRD NO	Intials	MAGNESIUM	PHOSPHORUS	VIRAL MARKERS	CHEST XRAY	USG W/A	NCCT HEAD	HRCT CHEST
42	1661520	BS	2.8	1.3	NON REACTIVE	RIGHT LOWER ZONE PATCH	NO SIGNIFICANT ABNORMALITY	-	-
43	1660685	RD	-	-	NON REACTIVE	NORMAL	NO SIGNIFICANT ABNORMALITY	-	-
44	1655373	MK	-	-	NON REACTIVE	CARDIOMEGALY		-	-
45	1631440	HK	-	-	NON REACTIVE	LEFT LOWER HAZINESS	SLLENOMEGALY , MILD LEFT PLEURAL EFFUSION	-	CONSOLIDATION IN BASAL SEGMENT OF LEFT LOWER LOBE
46	1441728	HS	2.5	1.82	NON REACTIVE	NORMAL	PROSTATOMEGALY	-	COPD
47	1163398	VS	2.8	2.6	NON REACTIVE	NORMAL	NO SIGNIFICANT ABNORMALITY	-	NO SIGNIFICANT ABNORMALITY
48	1686566	NS	-	-	NON REACTIVE	NORMAL	NO SIGNIFICANT ABNORMALITY	-	NO SIGNIFICANT ABNORMALITY
49	1609698	HS	-	-	NON REACTIVE	NORMAL	NO SIGNIFICANT ABNORMALITY	-	-
50	1639264	GK	-	-	NON REACTIVE	B/L BASAL HAZINESS	NO SIGNIFICANT ABNORMALITY	-	-

S.No.	MRD NO	Intials	2D ECHO	BONE MARROW ASPIRATION	BM ASPIRATE MUTATION	FLOWCYTOMETRY	BONE MARROW BIOPSY	PERIPHERAL BLOOD FLOWMETRY
42	1661520	BS	NORMAL LVEF=60%	PROMINENCE OF BLASTS CONSTITUTING 90% OF NUCLEATING CELLS	CBFB-MYH11	HLA DR 34 , CD 117 ,CD 13,CD33	AML- M4	-
43	1660685	RD	NORMAL LVEF=60%	PROMINENCE OF BLASTS CONSTITUING 82 % OF NUCLEATING CELLS	NPM 1	CD 117 , CD 13 , CD 33,CD123	AML-M0/M1	-
44	1655373	MK		PROMINENCE OF BLASTS CONSTITUING 66 % OF NUCLEATING CELLS	CBFB-MYH11	HLA DR, CD 34,CD 117,CD 13,CD38,CD123-AML	AML-M1	-
45	1631440	HK	NORMAL LVEF=60%	PROMINENCE OF BLASTS CONSTITUTING 80 % OF ALL NUCLEATED CELLS	AML PANEL NEGATIVE	HLA DR , CD34,CD117,CD13, CD 10 ,CD38,MPO-AML	AML-M2	-
46	1441728	HS	NORMAL LVEF=60%	PROMINENCE OF BLASTS CONSTITUTING 86 % OF ALL NUCLEATED CELLS	PML-RARA	CD 34,CD 117,CD 33,CD 13, CD64,CD123,MPO-AML	APML-M3	-
47	1163398	VS	NORMAL LVEF=60%	PROMINENCE OF BLASTS CONSTITUTING 95 % OF ALL NUCLEATED CELLS	NPM-1 ,FLT3-ITD	HLA DR ,CD 117,CD13,CD33,CD38,CD123,MPO-AML WITH MONOCYTIC DIFFERENTIATION	AML-M4	-
48	1686566	NS	NORMAL LVEF=60%	PROMINENCE OF ATYPICAL LYMPHOID CELLS - HAEMATOLYMPHOID MALIGNANCY	FLT3-D835	HLA DR ,CD 34, CD117,CD 13,CD38,CD123- AML	AML-M0	-
49	1609698	HS	CAD - RWMA WITH LVEF =42	PROMINRNCE OF BLASTS CONSTITUTING 90% OF ALL NUCLEATING CELLS	NPM 1	CD 117,CD33,MPO-AML	AML-M2	-
50	1639264	GK	NORMAL LVEF=60%	PROMINRNCE OF BLASTS CONSTITUTING 90% OF ALL NUCLEATING CELLS	AML PANEL NEGATIVE	HLA DR, CD 34,CD 117,CD 13,CD38,CD123,CD 33 ,MPO-AML WITH ABERRANT CD 7 EXPRESSION	AML-M2	-

			FINAL DIAGNOSIS	TREATMENT						
S.No.	**MRD NO**	**Intials**		**STARTED - YES/NO**	**HYPOMETHYLATING AGENTS (AZACYTIDINE,DECITABINE)**	**HYPOMETHYLATING AGENTS WITH VENETOCLAX**	**INTENSIVE CHEMOTHERAPY**	**PALLIATION**	**MEDICAL MANAGEMENT (ANTIBIOTICS)**	**EMPIRICAL ANTIFUNGALS STARTED**
42	1661520	BS	AML-M4	YES	AZACYTIDINE	-	-	-	YES	POSACONAZOLE
43	1660685	RD	AML	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	POSACONAZOLE
44	1655373	MK	ACYANOTIC CONGENITAL HEART DISEASE , AML	NO	-	-	-	-	YES	-
45	1631440	HK	AML	YES	-	-	DAUNORUBICIN PLUS CYTARABINE	-	YES	VORICONAZOLE
46	1441728	HS	APML WITH LRTI SEPSIS-FUNGAL, AKI	YES	-	-	ATO,ATRA	-	YES	MICAFUNGIN
47	1163398	VS	AML-MONOCYCTIC DIFFERENTATIATION	YES	-	-	DAUNORUBICIN PLUS CYTARABINE	-	YES	POSACONAZOLE
48	1686566	NS	AML	YES	AZACYTIDINE	VENETOCLAX	-	-	YES	VORICONAZOLE
49	1609698	HS	AML	NO	-	-	-	-	YES	-
50	1639264	GK	AML	YES	AZACYTIDINE	-	-	-	YES	VORICONAZOLE

			LENGTH OF HOSPITAL STAY	COMPLETE REMISSION YES/NO		FINAL OUTCOME				SATUS @ FOLLOWUP (AFETR 3MONTHS)	STATUS ON LAST FOLLOW UP(ALIVE/DIED)	
S.No.	**MRD NO**	**Intials**	**LENGTH OF HOSPITAL STAY**	**COMPLETE REMISSION YES/NO**	**ON BONE MARROW REMISSION**	**DISCHARGED**	**DISCHARGED ON REQUEST**	**DAMA**	**EXPIRED**			**SURVIVAL DAYS**
42	1661520	BS	4 DAYS			-	-	Yes	-	LOST TO FOLLOWUP	LOST TO FOLLOW UP	30
43	1660685	RD	7 DAYS	YES	90TH DAY	Yes	-	-	-	HEALTHY	MAY 2024 (DIED)	122
44	1655373	MK	3 DAYS			-	-	Yes	-	LOST TO FOLLOWUP	LOST TO FOLLOW UP	41
45	1631440	HK	30 DAYS	YES	30TH DAY	Yes	-	-	-	HEALTHY	APRIL 2024(ALIVE)	90
46	1441728	HS	32 DAYS	YES	30TH DAY	Yes	-	-	-	HEALTHY	SEP 2023 (ALIVE)	257
47	1163398	VS	34 DAYS	YES	8 TH MONTH	Yes	-	-	-	HEALTHY	MARCH 2023 (DIED)	942
48	1686566	NS	15 DAYS	-	-	Yes	-	-	-	LOST TO FOLLOWUP	LOST TO FOLLOW UP	20
49	1609698	HS	13 DAYS	-	-	-	-	Yes	-	HEALTHY	FEB 2024 (ALIVE)	231
50	1639264	GK	15 DAYS	-	-	Yes	-	-	-	HEALTHY	MAY 2024 (ALIVE)	287

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The Principal
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Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Gurinderjit Singh**, a student of your college for **MD General Medicine** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Clinical spectrum and short-term outcome of acute myeloid leukemia patients .

Supervisor	**Co-Supervisor:-**	**Co-Supervisor:-**
Dr. Gautam Ahluwalia Professor Dept. of General Medicine	Dr. Suvir Singh Assoc. Prof. & Head, Dept. of Hematology & Stem Cell Transplantation,	Dr. Vikram Narang Assoc. Professor Dept. of Pathology

The student may submit the thesis in triplicate alongwith the plan in duplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

CLINICAL SPECTRUM AND SHORT-TERM OUTCOME OF ACUTE MYELOID LEUKEMIA PATIENTS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

AUGUST, 2022 **DR. GURINDERJIT SINGH**

DEPARTMENT OF GENERAL MEDICINE
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	CLINICAL SPECTRUM AND SHORT-TERM OUTCOME OF ACUTE MYELOID LEUKEMIA PATIENTS
For the degree of	MD General Medicine
Name of the candidate	Dr. Gurinderjit Singh
Supervisor	Dr. Gautam Ahluwalia, Professor, Department of General Medicine
Co-Supervisor	Dr. Suvir Singh, Associate Professor & Head, Department of Hematology & Stem Cell Transplantation Dr. Vikram Narang, Associate Professor, Department of Pathology
Institution	Dayanand Medical College and Hospital,Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

INTRODUCTION: Acute myeloid leukemia (AML) is collection of neoplastic blood disorders categorized by the proliferation and growth of immature hematopoietic cells in the bone marrow and blood. The higher incidence of AML is seen in adults, accounting for almost 80 % of acute leukemia in adults and only 20 % of acute leukemia in children. It is most commonly found acute leukemia in adults. AML is actually a varied selection of wide number of malignant neoplastic diseases that may be grouped on the basis of morphological, cytogenetic and also with molecular and genetics criteria.

AIMS AND OBJECTIVES: To study the clinical spectrum and short-term outcome of acute myeloid leukemia patients admitted in a tertiary care hospital.

MATERIALS & METHODS: A prospective observational study will be conducted in adults patients admitted with acute myeloid leukemia in DMCH, Ludhiana. The study duration will be from 1st October 2022 to 31st March 2024.

CLINICAL SIGNIFICANCE: AML is most commonly found acute leukemia in adults. The developing countries have greater burden of cancer including hematological malignancies due to population growth, aging and urbanization, changing dietary habits, better control of infections and increasing tobacco consumption. In a resource-limited setting like our country, there is a paucity of epidemiological data about this life threatening hematological malignancy. This study is aimed at delineating the clinical features, pathological spectrum and short-term outcome of AML in patients admitted in tertiary care teaching hospital.

Keywords: Prospective, Acute Myeloid Leukemia, Clinical Profile, Short Term Outcome In Adult Patients

(Signature) Candidate | (Signature) Co-supervisor | (Signature) Co-supervisor | (Signature) Supervisor | (Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"CLINICAL SPECTRUM AND SHORT-TERM OUTCOME OF ACUTE MYELOID LEUKEMIA PATIENTS"** exist in the Department of General Medicine at Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate himself under our supervision and guidance.

Supervisor

Dr. Gautam Ahluwalia
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Dr. Dinesh Gupta
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Place : LUDHIANA

Date : 1/10/22

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Gurinderjit Singh
Department	General Medicine
Topic of Thesis	CLINICAL SPECTRUM AND SHORT-TERM OUTCOME OF ACUTE MYELOID LEUKEMIA PATIENTS
Likely date of appearing in PG examination	May/June, 2024
Date of enrollment	March 4, 2022
Name of Head of Department	Dr. Dinesh Gupta
1) Supervisor **2) Co-Supervisors**	Dr. Gautam Ahluwalia Dr. Suvir Singh Dr. Vikram Narang
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1.	NAME OF THE CANDIDATE AND ADDRESS	DR. GURINDERJIT SINGH WARD NO 8 BEHLOLPUE ROAD NEAR DR JAMEEL, SAMRALA LUHDIANA, SAMRALA
2.	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA
3.	COURSE OF STUDY AND SUBJECT	M.D. GENERAL MEDICINE
4.	DATE OF ADMISSION OF COURSE	4TH MARCH 2022
5.	TITLE OF THE TOPIC	CLINICAL SPECTRUM AND SHORT-TERM OUTCOME IN ACUTE MYELOID LEUKEMIA PATIENTS

6.BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Acute myeloid leukemia (AML) is collection of neoplastic blood disorders categorized by the proliferation and growth of immature hematopoietic cells in the bone marrow and blood. The higher incidence of AML is seen in adults, accounting for almost 80 % of acute leukemia in adults and only 20 % of acute leukemia in children. AML is actually a varied selection of wide number of malignant neoplastic diseases that may be grouped on the basis of morphological, cytogenetic and also with molecular and genetics criteria.

Depending upon the etiology, genetics, immune-phenotype, and morphology, there are different classification systems for AML.The most common risk factor for AML is myelodysplastic syndrome. Other hematological disorders that increase the risk of AML include myelofibrosis and aplastic anemia. Several congenital disorders like Down syndrome and Bloom syndrome also increase the risk of AML, which tends to present in the early 20s.Environmental exposures like radiation, tobacco smoke and benzene are also risk factors for AML.

Finally, previous exposure to chemotherapeutic agents is also a risk factor for AML.AML should be suspected in anyone with unexplained cytopenias (decreased cell count of white blood cells, hemoglobin, or platelets), the presence of circulating blast cells in the peripheral blood, easy bruising or bleeding or recurrent infections. In some cases, they can present with renal failure secondary to tumor lysis syndrome which is an oncologic emergency.[1-2]

Individuals who achieve complete remission (CR) with a blast count of less than 5% in the bone marrow after induction therapy tend to have increased survival. Despite induction therapy, there is still minimal residual disease for which consolidation therapy is initiated to prevent any risk of relapse by eliminating the residual disease. Despite many advances, the

mainstay of therapy remains a combination of cytarabine-based and anthracycline-based regimens. For eligible candidates, allogeneic stem cell transplantation should be considered.[3-4]

The developing countries have greater burden of cancer including hematological malignancies due to population growth, aging and urbanization, changing dietary habits, better control of infections and increasing tobacco consumption. In a resource-limited setting like our country, there is a paucity of epidemiological data about this life-threatening hematological malignancy. This study is aimed at delineating the clinical features, pathological spectrum and short-term outcome of AML in patients admitted in a tertiary care teaching hospital.

6.2 REVIEW OF LITERATURE

Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy characterized by clonal expansion of myeloid blasts in the peripheral blood, bone marrow, and/or other tissues, which leads to impaired production of normal blood cells. Thus, leukemic cell infiltration in the marrow invariably leads to bone marrow failure manifesting in the form of anemia or thrombocytopenia, while absolute neutrophil count may be low or normal, depending on the total white cell count.[5]

The underlying pathophysiology in AML consists of a maturational arrest of bone marrow cells in the earliest stages of development. The mechanism of this arrest is under study, but in many cases, it involves the activation of abnormal genes through chromosomal translocations and other genetic abnormalities.[6-7] Those genetic changes can be inherited or acquired to some environmental insult. AML accounts for approximately 20% of acute leukemia in children and 80% of acute leukemia in adults. The incidence of AML progressively increases with age, and in adults over the age of 65 years, the incidence is approximately 30 times the incidence of AML in children. The highest rate of childhood AML is in Asia and the lowest in North America and India.[8] As per the SEER database, the number of new cases of AML was 4.2 per 100,000 men and women per year. The number of deaths was 2.8 per 100,000 men and women per year. These rates are age adjusted and based on 2010–2014 cases and deaths. AML is most frequently diagnosed among people aged 65–74 years. Median age at diagnosis is 68 years.[9]

In the past, the French-American-British system classified AML into eight subtypes, FAB M0 to M7, which are as follows:

- M0: Undifferentiated AML
- M1: AML with minimal maturation
- M2: AML with maturation
- M3: Acute promyelocytic leukemia (APL)
- M4: Acute myelomonocytic leukemia
- M5: Acute monocytic leukemia
- M6: Acute erythroid leukemia
- M7: Acute megakaryocytic leukemia

The newer who classification is based on molecular markers and morphology [Table 1].[10] The European Leukemia Network has divided AML into three risk groups, as favorable risk, intermediate risk, and poor risk groups [Table 2].[11]

Table 1:WHO classification of acute myeloid leukemia

AML and related neoplasms

AML with recurrent genetic abnormalities

AML with t(8;21)(q22;q22.1); RUNX1-RUNX1T1

AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11

APL with PML-RARA

AML with t(9;11)(p21.3;q23.3);MLLT3-KMT2A

AML with t(6;9)(p23;q34.1);DEK-NUP214

AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2, MECOM

AML (megakaryoblastic) with t(1;22)(p13.3;q13.3); RBM15-MKL1

AML with mutated NPM1

AML with biallelic mutations of CEBPA

AML with myelodysplasia‑related changes

Therapy-related myeloid neoplasms

AML, NOS

AML with minimal differentiation

AML without maturation

AML with maturation

Acute myelomonocytic leukemia

Acute monoblastic/monocytic leukemia

Pure erythroid leukemia

Acute megakaryoblastic leukemia

Acute basophilic leukemia

Acute panmyelosis with myelofibrosis

Myeloid sarcoma

Myeloid proliferations related to down syndrome

TAM

Myeloid leukemia associated with down syndrome

AML – Acute myeloid leukemia APL – Acute promyelocytic leukemia; NOS – Not otherwise specified; TAM – Transient abnormal myelopoiesis

Table 2: 2017 European leukemia net risk stratification of acute myeloid leukemia by genetics

Risk category*	Genetic abnormality
Favorable	t(8;21)(q22;q22.1); RUNX1-RUNX1T1
	Inv(16)(p13.1;q22) or t(16;16)(p13.1;q22); CBFB-MYH11
	Mutated NPM1 without FLT3-ITD or with FLT3-ITD
	Biallelic mutated CEBPA
Intermediate	Mutated NPM1 and FLT3-ITDhigh
	Wild-type NPM1 without FLT3-ITD or with FLT3-ITDlow (without adverse-risk genetic lesions)
	t(9;11)(p21.3;q23.3); MLLT3-KMT2A
	Cytogenetic abnormalities not classified as favorable or adverse
Adverse	t(6;9)(p23;q34.1); DEK-NUP214
	t(v; 11q23.3); KMT2A rearranged
	t(9;22)(q34.1;q11.2); BCR-ABL1
	Inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2, MECOM(EVI1) −5 or del (5q); −7; −17/abn(17p)
	Complex karyotype, monosomal karyotype
	Wild-type NPM1 and FLT3-ITDhigh
	Mutated RUNX1
	Mutated ASXL1
	Mutated TP53

Treatment is individualized as we have to distinguish M3 from non M3 at the outset. For non M3, induction is given which consists of mainly daunorubicin and cytarabine. Dosages of daunorubicin range from 45 to 90 mg/m2 given day 1–day 3, while cytarabine dosage is 100–200 mg/m2 given by 24 h infusion over 7 days. Recent studies have clearly shown dose of 60 mg/m2 better than 45 mg/m2 , and then further, Burnett et al. have clearly shown 60 mg/m2 better than 90 mg/m2 in terms of same complete remission (CR) and lower 60 day mortality. Idarubicin can also be used in the place of daunorubicin with the same outcome. CR rates in the age group of <50 years have consistently been in the range of 60%–70% in largest cooperative group trials of infusional cytarabine and anthracyclines. Induction is followed by consolidation once remission is documented. Type of treatment mainly depends upon risk stratification. Adverse-risk patients are taken for allogenic stem cell transplant. Favorable-risk patientsare to be taken for 3–4 cycles of high dose cytarabine. Intermediate risk patients are to be given either allogenic stem cell transplant or high dose cytarabine depending upon the availability of donor and age of patient. Patients who fall in M3 type (acute promyelocytic leukemia [APML]) need differentiating agent as induction treatment. These agents are all transretinoic acid (ATRA) and arsenic trioxide which are combined with conventional chemotherapy agents. Most of the studies mention CR rate of around 90%. Transplant is only used in relapsed setting.[12]

PROGNOSIS

By assessing the prognostic factors, clinicians can decide whether a standard therapy or more intense therapy would be helpful in maintaining CR and OS rates. The prognostic factors are chromosomal abnormalities (favorable abnormalities include t(8;21), t(15;17), inversion of chromosome 16), genetic mutations (NPM1 gene has a favorable prognosis, and FLT3 gene has unfavorable prognosis). Worse outcomes

have been noted with older age, white blood cell count greater than 100,000 at the time of diagnosis, s-AML, t-AML, the presence of leukemic cells in the central nervous system (CNS).

6.3 AIMS AND OBJECTIVES OF THE STUDY

- To study the clinical spectrum and short-term outcome of acute myeloid leukemia patients admitted in a tertiary care hospital.

7. MATERIAL AND METHODS

7.1 SOURCE OF DATA

All the patients aged more than 18 years admitted with acute myeloid leukemia in Department of Medicine and allied Specialties of Dayanand Medical College and Hospital (DMCH), Ludhiana

7.2 METHOD OF COLLECTION OF DATA

Study Population

A prospective observational study will be conducted in adults patients admitted with acute myeloid leukemia in DMCH, Ludhiana. The study duration will be from 1st October 2022 to 31st March 2024.

Inclusion Criteria

- Age $\geq$ 18 years.
- Diagnosed cases of acute myeloid leukemia admitted in department of Medicine and allied Specialties

Exclusion Criteria

- Age < 18 years.
- Patients not giving consent for enrollment in the study.

OUTCOME

- Length of stay in hospital.
- Clinical/laboratory/treatment profile of admitted patients.
- Details of pre admission workup and treatment outside (wherever available)
- Documentation of complete hematologic remission and bone marrow remission after induction on bone marrow
- Outcome of the treatment and the type of treatment received (standard treatment or supportive care)
- Follow-up post-discharge (wherever feasible) at 3 months

Statistical Analysis:

The data will be analyzed statistically using appropriate methodology. Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Investigations considered necessary by the treating unit/department will be evaluated. The investigations will be broadly divided into the following groups:

- Basic investigations: CBC, LFT, RFT, Urine routine, inflammatory markers like ESR, LDH, CRP and/or any other
- Specific investigations:
    - Bone marrow aspiration and biopsy for morphology, cytochemistry, flow cytometry and cytogenetics by conventional karyotyping and/or any other technique
    - Molecular analysis using a targeted allele specific PCR or next generation sequencing for myeloid mutations (as feasible)
- Radiological investigations: Chest radiograph, US, CT Scan, MRI and/or PET scan
- Detailed proforma format is attached herewith with thesis plan

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes. Attached herewith.

8. LIST OF REFERENCES

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2. Boddu, P.C. and Zeidan, A.M., 2019. Myeloid disorders after autoimmune disease. Best Practice & Research Clinical Haematology, 32, pp.74-88.
3. Liu XJ, Huang XJ, Xu LP, Liu KY, Zhang XH, Yan CH, et al. [Effects of pre-transplant course on prognosis of allogeneic hematopoietic stem cell transplantation in patients with acute myeloid leukemia]. ZhonghuaXue Ye Xue Za Zhi. 2019;40:182-86.
4. Leisch, M., Jansko, B., Zaborsky, N., Greil, R. and Pleyer, L., 2019. Next generation sequencing in AML—on the way to becoming a new standard for treatment initiation and/or modulation?. Cancers, 11, p.252.
5. Lichtman MA, Beutler E, Kipps TJ, Seligsohn U, Kaushansky K. Acute myelogenous leukemia. Williams Hematology. Malignant Diseases. Part IX. 7th ed., Ch. 87. McGraw-Hill: 2006 1183-236.
6. Vardiman JW, Harris NL, Brunning RD. The World Health Organization (WHO) classification of the myeloid neoplasms. Blood 2002;100:2292-302.
7. Smith MT, Skibola CF, Allan JM, Morgan GJ. Causal models of leukaemia and lymphoma. IARC Sci Publ 2004;157:373-92.
8. Ghosh S, Shinde SC, Kumaran GS, Sapre RS, Dhond SR, Badrinath Y, et al. Haematologic and immunophenotypic profile of acute myeloid leukemia: An experience of Tata memorial hospital. Indian J Cancer. 2003;40:71-6.
9. Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Kosary CL, et al, editors. SEER Cancer Statistics Review, 1975 2014. Bethesda, MD: National Cancer Institute.

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12. NCCN Clinical Practice Guidelines in Oncology. Acute Myeloid Leukemia: Version 1. 2017. National Comprehensive Cancer Network.

PROFORMA

S. No.

Name MRD No.

Age/ Gender

Father's Name

Address

Occupation

Date of Admission

Date of Discharge

Provisional Diagnosis

Date of Diagnosis of AML

Presenting Complaints And Duration

EXAMINATION

Height Weight

Body surface area

Pulse Rate

Blood Pressure

Respiratory Rate

Temperature

Cyanosis

Clubbing

Icterus

Pallor

Petechiae/ Purpura/any other skin abnormalities

JVP

SYSTEMIC EXAMINATION

1.Respiratory System

2. Abdominal examination

3. Cardiovascular System

4. Central Nervous System

INVESTIGATIONS

CBC

PBF EXAMINATION

Blood Sugar

RFT

LFT

PTI/ INR

aPTT

CALCIUM, PHOSPHORUS, Magnesium

URIC ACID

VIRAL MARKERS

ESR

SERUM LDH

Blood culture

Chest X ray

USG Abdomen

CT Thorax + Upper abdomen

MRI Brain + Spinal Cord

ECG

ECHO

CSF analysis

WB PET CT Scan

BONE MARROW STUDIES

-Aspiration

-BM Aspirate for flow cytometry: Acute leukemia

- BM aspirate for molecule markets by RT-PCR: FLT-3 gene mutation , NPM-1 gene mutation ,CEBPA gene mutation

-BM Aspirate for conventional cytogenetics (Karyotyping)

-BM biopsy

NGS panel for myeloid neoplasms if performed

Risk stratification

Final Diagnosis

Treatment Started – Yes / No

Treatment Plan / Given:

Treatment given –

- Hypomethylating Agents (azacytidine,decitabine)
- Hypomethylating agents with Venetoclax
- Intensive chemotherapy
- Palliation treatment

Day 14th bone marrow biopsy -Yes /no

Febrile neutropenia -Yes/no

Blood Culture

Radiological Investigations

CXR

HRCT Chest

Empirical antifungals – voriconazole

– posaconazole

Complete Remission -Yes/No

If yes Date-

Day 30th

Day 60th

Day 90th

Day of last follow up-

Outcome –

Indoor patients – Discharge / DAMA / Death

Status at last follow up-

SIGNATURE OF CANDIDATE **SIGNATURE OF CO-SUPERVISOR**

SIGNATURE OF CO-SUPERVISOR

SIGNATURE OF SUPERVISOR

INFORMED PATIENT CONSENT

Date: _____

I…… D/o, W/o, S/o……. am willing to participate in the study **"CLINICAL SPECTRUM AND SHORT-TERM OUTCOME OF ACUTE MYELOID LEUKEMIA PATIENTS"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

…… ……

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Co-Supervisor**

Signature of Co-Supervisor

Signature of Supervisor

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____
निवासी _____
इस शोधकार्य "**CLINICAL SPECTRUM AND SHORT-TERM OUTCOME OF ACUTE MYELOID LEUKEMIA PATIENTS"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____	_____
गवाह के हस्ताक्षर	रोगी के हस्ताक्षर/अंगूठे का निशान
नाम:	नाम:

_____
विद्यार्थी के हस्ताक्षर

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सह-अन्वेषक के हस्ताक्षर

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सह-अन्वेषक के हस्ताक्षर

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अन्वेषक के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“CLINICAL SPECTRUM AND SHORT-TERM OUTCOME OF ACUTE MYELOID LEUKEMIA PATIENTS” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ

_____

ਸਹਿ-ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਹਿ-ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ